Transition Metal Free C-N Bond Forming Dearomatizations and Aryl C-H Aminations by In Situ Release of a Hydroxylamine-Based Aminating Agent

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Supporting Information

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General Experimental Details. Starting materials were purchased from commercial sources (Acros, Aldrich, Alfa Aesar) and used without further purification unless otherwise stated. Anhydrous 2,2,2-trifluoroethanol was obtained by drying over 4Å molecular sieves while other anhydrous solvents were obtained by passage through drying columns supplied by Anhydrous Engineering Ltd. The removal of solvents *in vacuo* was achieved using both a Büchi rotary evaporator (bath temperatures up to 45 °C) at a pressure of either 15 mmHg (diaphragm pump) or 0.1 mmHg (oil pump), as appropriate, and a high vacuum line at r.t.. Reactions requiring anhydrous conditions were run under a dry atmosphere of nitrogen or argon; glassware was either flame dried immediately prior to use or placed in an oven (200 °C) for at least 2 h and allowed to cool either in a desiccator or under an atmosphere of nitrogen or argon; liquid reagents, solutions or solvents were added via syringe through rubber septa. Flash column chromatography was performed using silica gel (Aldrich 40-63 μm, 230-400 mesh). Thin layer chromatography was performed using aluminium backed $60F_{254}$ silica plates. Visualisation was achieved by UV fluorescence or a basic $KMnO_4$ solution and heat. Proton nuclear magnetic resonance were recorded on a Varian or Jeol spectrometer at 400 MHz or 500 MHz while ^{13}C NMR spectra were recorded at 100 MHz. Chemical shifts (δ) are given in parts per million (ppm) and referenced to the appropriate residual solvent peak. Peaks are described as singlets (s), doublets (d), triplets (t), quartets (q), quintets (qn), sextets (s), multiplets (m) and broad (br.). Coupling constants (*J*) are quoted to the nearest 0.1 Hz. Assignments of ^{1}H NMR and ^{13}C NMR signals were made, where possible, using COSY, HSQC, HMBC, NOE and TOCSY experiments. Mixtures of isomers which could not be separated (e.g. diastereomers and/or rotamers) have been characterized together and are referred to as A and B. Numbering systems for NMR signal assignments are specified on the structure and are not related to those used for the compound names. In situ yields were determined by integration of the ^{1}H NMR of the crude material employing 1,3,5-trimethoxybenzene or 1,4-dinitrobenzene as internal standard. Mass spectra were determined by the University of Bristol mass spectrometry service using a Bruker Daltonics FT-ICR-MS Apex 4e 7.0T FT-MS. Infrared spectra were recorded on a Perkin Elmer Spectrum Two FTIR spectrometer as either neat films or solids. Abbreviations used are: w (weak), m (medium), s (strong) and br (broad). Melting points were determined using a Reichert melting point table and temperature controller and are uncorrected.

Experimental procedures and Data

General procedure A for TBS protection of phenol

To a solution of alcohol (1.0 eq.) in DMF (*approx*. 2mL/mmol) at 0 °C was added imidazole (3.3 eq.) and *tert*-butyldimethylsilyl chloride (2.2 eq.). The reaction was stirred at r.t. and monitored by TLC. Upon completion, the reaction was quenched by addition of H_2O and the organic phase extracted with hexane, dried over Na_2SO_4 and concentrated *in vacuo*. To the crude reaction mixture was added MeOH (1 mL/mmol), THF (1 mL/mmol) and aq. K_2CO_3 (2.0 eq.) After stirring for 12 h the reaction was quenched with aq. 1 M HCl at 0 °C (until pH *approx*. 3). The mixture was extracted with Et_2O (3 × 20 mL), dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude reaction mixture was purified by flash column chromatography.

General procedure B for reduction of carboxylic acid/ester to alcohol using $LiAlH_4$

To a solution of carboxylic acid/ester (1.0 eq.) in anhydrous THF or Et_2O (*approx*. 5 mL/mmol) at 0 °C was added $LiAlH_4$ (*equivalents specified*) dropwise. The reaction was stirred at r.t. and monitored by TLC. Upon completion, the reaction mixture was cooled to 0 °C before addition of water (1 mL/g of $LiAlH_4$), 15% aq. NaOH (1 mL/g $LiAlH_4$) and a final portion of water (3 mL/g of $LiAlH_4$). The mixture was filtered through Celite® and washed with CH_2Cl_2. The phases were separated and the aqueous phase extracted with CH_2Cl_2 (2 × 10 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated *in vacuo* to afford the crude product which was purified by flash column chromatography.

General procedure C for preparation of hydroxylamine derivatives by Mitsunobu reaction[1]

Diisopropyl azodicarboxylate (1.2 eq.) was added at 0 °C to a stirring solution of triphenylphosphine (1.2 eq.) in anhydrous THF (*approx*. 2mL/mmol) under a nitrogen atmosphere. After 30 min stirring at this temperature a solution of alcohol (1.0 eq.) and amine nucleophile (1.2 eq.) in anhydrous THF (*approx*. 2mL/mmol) were added. The reaction was stirred at 0 °C for 1 h after which it was stirred at r.t. and monitored by TLC. Upon completion, the reaction mixture was concentrated *in vacuo* and purified by flash column chromatography.

General procedure D for removal of silyl protecting group with TBAF/AcOH

To a solution of silyl ether (1.0 eq.) in THF (*approx*. 20mL/mmol) at 0 °C was added a solution of 1:1 TBAF/AcOH (*equivalents specified*, 0.1 M in THF). The reaction mixture was stirred at r.t. and monitored by TLC. Upon completion, the reaction mixture was quenched with water (10 mL), extracted with EtOAc (2 × 10 mL), washed with sat. aq. $NaHCO_3$ (10 mL) and brine (10 mL), dried over Na_2SO_4, filtered and the concentrated *in vacuo*. The crude product was purified by flash column chromatography.

General procedure E for intramolecular dearomatizing amination

To a stirring solution of Boc-protected amino substrate (1.0 eq.) in anhydrous 2,2,2,-trifluoroethanol (0.1 M) at 0 °C was added trifluoroacetic acid (2.0 eq.). After stirring for 2 h at 0 °C the reaction was warmed to r.t. and monitored by TLC. Upon completion, the reaction mixture was concentrated *in vacuo* and purified by flash column chromatography, with a small amount of Et_3N (<1%) added to the appropriate eluent. In cases where the product was unstable the TFA salt was obtained by re-acidification with TFA.

General procedure F for formation of unsaturated esters by Wittig reaction

Aldehyde (1.0 eq.) and methyl 2-(triphenyl-phosphaneylidene) acetate or ethyl 2-(triphenyl-phosphaneylidene) acetate (1.5 eq.) in CH_2Cl_2 (*approx*. 1 mL/mmol) were stirred at r.t. overnight and monitored by TLC. Upon completion, the reaction mixture was concentrated *in vacuo* and purified by flash column chromatography.

General procedure G for alkene hydrogenation with Pd/C

A solution of alkene (1.0 eq.) in MeOH or EtOH or EtOAc (*approx*. 5 mL/mmol) was purged with argon before the addition of 10 wt. % Pd/C (5-10 mol%). The flask was fitted with a balloon of hydrogen and stirred at r.t. overnight and monitored by TLC. Upon completion, the reaction mixture was filtered over a bed of Celite® washing with the appropriate solvent and concentrated *in vacuo* to afford the product

General Procedure H for preparation of Weinreb amides from Carboxylic acids

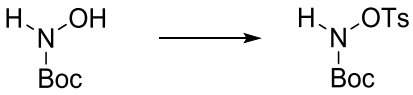
To a solution of carboxylic acid (1.0 eq.) in anhydrous CH_2Cl_2 under nitrogen at 0 °C was added *N*,*O*-dimethylhydroxylamine hydrochloride (1.4 eq.), Et_3N (1.4 eq.), 4-dimethylaminopyridine (1.4 eq.), and *N*,*N*'-dicyclohexylcarbodiimide (1.4 eq.). The solution was stirred at r.t. overnight and then filtered through Celite, eluting with EtOAc. The filtrate

was washed sequentially with 1 M aq. HCl (10 mL) and sat. aq. $NaHCO_3$ (10 mL). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude product was purified by flash column chromatography.

General procedure I for reduction of carboxylic acids to alcohols *via* anhydride

To a solution of carboxylic acid (1.0 eq.) and triethylamine (1.0 eq.) in THF (10 mL/mmol) at -5 °C was added a solution of ethyl chloroformate (1.0 eq.) in THF (1 mL/mmol) dropwise maintaining a temperature below 0 °C. The reaction was stirred at the same temperature for 1 h and filtered to remove the white precipitate that formed, washing with THF (10 mL). The filtrate was added dropwise to a solution of $NaBH_4$ (2.5 eq.) in H_2O (*approx*. 2 mL/mmol) at -5 °C. The reaction was stirred at r.t. overnight and monitored by TLC. Upon completion, the reaction was acidified to approx. pH 3 with aq. 1 M HCl. The layers were separated and the aqueous layer extracted with Et_2O (3 × 10 mL). The combined organic extracts were washed with aq. 1 M NaOH (10 mL) and H_2O (10 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude product was purified by flash column chromatography.

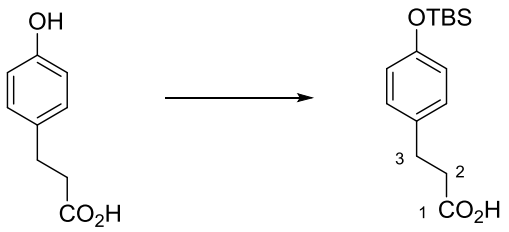
***tert*-Butyl (tosyloxy)carbamate (4)**[2]



The title compound was prepared according to a literature procedure.[2]

The spectroscopic properties were consistent with the data available in the literature.[2]

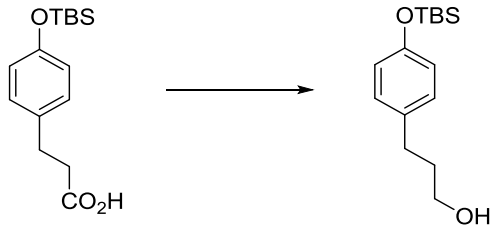
3-(4-((*tert*-Butyldimethylsilyl)oxy)phenyl)propanoic acid[3]



General procedure A: 3-(4-Hydroxyphenyl)propanoic acid (8.30 g, 50.0 mmol), *tert*-butyldimethylsilyl chloride (16.5 g, 110.0 mmol) and imidazole (11.25 g, 165.0 mmol) in DMF

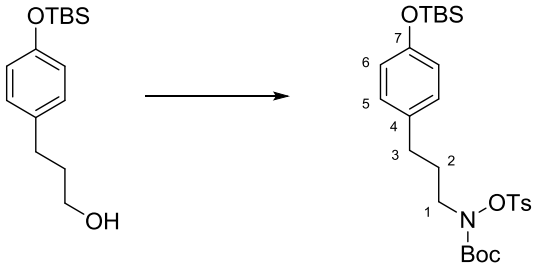
(100 mL) were employed. Purification by flash column chromatography (25 % EtOAc/hexane) afforded the title compound (10.8 g, 77 %) as a colorless solid; m.p.: 69 - 71 ^{o}C (EtOAc/hexane); R_f = 0.2 (20 % EtOAc/hexane); ν_{max} / cm^{-1} (solid) 2926 (m), 2882 (m), 2855 (m), 1714 (s), 1509 (s), 1249 (s), 1213 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.30 (1H, br s, COO<u>H</u>), 7.06 (2H, d, *J* = 8.3 Hz, ArC<u>H</u>), 6.77 (2H, d, *J* = 8.3 Hz, ArC<u>H</u>), 2.89 (2H, t, *J* = 7.6 Hz, C**3**-<u>H</u>$_2$), 2.65 (2H, t, *J* = 7.3 Hz, C**2**-<u>H</u>$_2$), 0.99 (9H, s, TBS (C<u>H</u>$_3$)$_3$), 0.19 (6H, s, TBS (C<u>H</u>$_3$)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 179.4 (C**1**), 154.2 (Ar<u>C</u>), 133.0 (Ar<u>C</u>), 129.3 (2 x Ar<u>C</u>H), 120.2 (2 x Ar<u>C</u>H), 36.1 (C**2**), 30.0 (C**3**), 25.8 (TBS (<u>C</u>H$_3$)$_3$), 18.3 (TBS Si<u>C</u>(CH$_3$)$_3$), -4.3 (TBS Si(C<u>H</u>$_3$)$_2$). HRMS (ESI$^+$) Calculated for $C_{15}H_{25}O_3Si$: 281.1567. Found [M+H]$^+$: 281.1580. *The title compound has been described only in a patent.*[3]

3-(4-((*tert*-Butyldimethylsilyl)oxy)phenyl)propan-1-ol[4]



General procedure B: 3-(4-((*tert*-Butyldimethylsilyl)oxy)phenyl)propanoic acid (1.40 g, 5.0 mmol) and 2.0 eq. $LiAlH_4$ (1M in THF) in anhydrous Et_2O were employed. Purification by flash column chromatography (25 % EtOAc/hexane) afforded the title compound (0.99 g, 74 %) as a colorless oil R_f = 0.6 (33% EtOAc/hexane); ν_{max} / cm^{-1} (film) 3339 (br m), 2929 (s), 2885 (s), 2858 (s), 1609 (m), 1508 (s), 1250 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04 (2H, d, *J* = 8.0 Hz), 6.75 (2H, d, *J* = 8.0 Hz), 3.64-3.68 (2H, m), 2.64 (2H, t, *J* = 7.4 Hz), 1.86 (2H, m), 1.35, (1H, br s), 0.98 (9H, s), 0.18 (6H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.7, 134.4, 129.2, 119.9, 62.3, 34.4, 31.2, 25.7, 18.2, -4.4. *Spectroscopic properties were consistent with the data available in the literature.*[4]

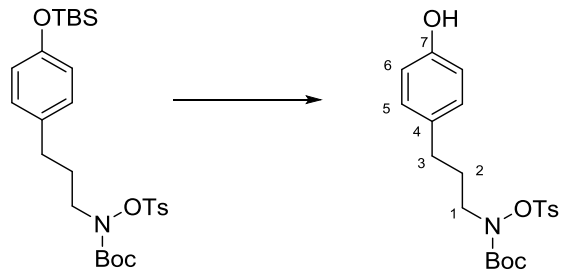
***tert*-Butyl (3-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)propyl)(tosyloxy)carbamate (*silyl*-5a)**



***silyl*-5a**

General procedure C: 3-(4-((*tert*-Butyldimethylsilyl)oxy)phenyl)propan-1-ol (0.79 g, 3.00 mmol), PPh_3 (0.94 g, 3.60 mmol), DIAD (0.71 mL, 3.60 mmol) and TsONHBoc (1.03 g, 3.60 mmol) in THF (12 mL) were employed. Purification by flash column chromatography (10 % EtOAc/hexane) afforded ***silyl*-5a** (1.49 g, 93 %) as a pale yellow oil; R_f = 0.5 (20 % EtOAc/hexane); ν_{max} / cm^{-1} (film) 2955 (m), 2930 (m), 2858 (m), 1753 (m), 1720 (s), 1509 (s), 1382 (s), 1368 (s), 1251 (s), 1178 (s), 1154 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (2H, d, *J* = 8.3 Hz, Ts ArC<u>H</u>), 7.33 (2H, d, *J* = 8.3 Hz, Ts ArC<u>H</u>), 7.00 (2H, d, *J* = 8.4 Hz, C**5**-<u>H</u>), 6.74 (2H, d, *J* = 8.4 Hz, C**6**-<u>H</u>), 3.60 (2H, app. br s, C**1**-<u>H_2</u>), 2.52 (2H, t, *J* = 7.8 Hz, C**3**-<u>H_2</u>), 2.45 (3H, s, Ts C<u>H_3</u>), 1.95 - 1.85 (2H, m, C**2**-<u>H_2</u>), 1.22 (9H, s, Boc (C<u>H_3</u>)$_3$), 0.98 (9H, s, TBS (C<u>H_3</u>)$_3$), 0.18 (6H, s, TBS (C<u>H_3</u>)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.5 (C=O), 153.8 (C**7**), 145.6 (Ts Ar<u>C</u>), 133.7 (C**4**), 131.3 (Ts Ar<u>C</u>), 129.6 (2 × Ts Ar<u>C</u>H), 129.5 (2 × Ts Ar<u>C</u>H), 129.1 (C**5**), 120.0 (C**6**), 83.2 (Boc <u>C</u>(CH$_3$)$_3$), 52.6 (C**1**), 32.0 (C**3**), 27.6 (Boc (<u>C</u>H$_3$)$_3$), 27.5 (C**2**), 25.7 (TBS (<u>C</u>H$_3$)$_3$), 21.7 (Ts <u>C</u>H$_3$), 18.2 (TBS Si<u>C</u>(CH$_3$)$_3$), -4.4 (TBS Si(<u>C</u>H$_3$)$_2$); HRMS (ESI$^+$) Calculated for $C_{27}H_{41}NNaO_6SSi$: 558.2316. Found $[M+Na]^+$: 558.2313.

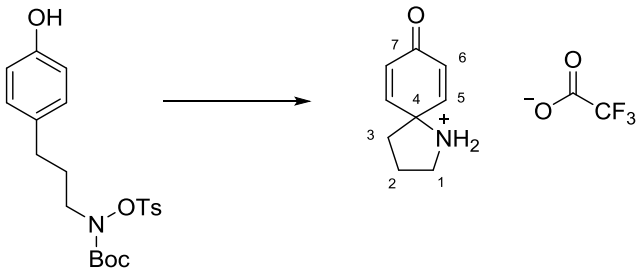
***tert*-Butyl (3-(4-hydroxyphenyl)propyl)(tosyloxy)carbamate (5a)**



silyl-5a **5a**

General procedure D: *tert*-Butyl (3-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)propyl) (tosyloxy)carbamate (***silyl*-5a)** (0.69 g, 1.28 mmol) and 1:1 TBAF/HOAc solution (0.1 M in THF, 1.28 mmol) in THF (20 mL) were employed. Purification by flash column chromatography (20 % EtOAc/hexane) afforded **5a** (0.35 g, 60 %) as a colorless solid; m.p.: 63 - 65 ^{o}C (EtOAc/hexane); R_f = 0.2 (20 % EtOAc/hexane); ν_{max} / cm^{-1} (solid) 3426 (m, br), 2982 (m), 2934 (m), 1721 (s), 1515 (s), 1369 (s), 1191 (s), 1177 (s), 1152 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (2H, d, *J* = 8.3 Hz, Ts ArC<u>H</u>), 7.32 (2H, d, *J* = 8.3 Hz, Ts ArC<u>H</u>), 6.98 (2H, d, *J* = 8.4 Hz, C**5**-<u>H</u>), 6.75 (2H, d, *J* = 8.4 Hz, C**6**-<u>H</u>), 5.75 (1H, br s, O<u>H</u>), 3.60 (2H, app. br s, C**1**-<u>H_2</u>), 2.50 (2H, t, *J* = 7.8 Hz, C**3**-<u>H_2</u>), 2.44 (3H, s, Ts C<u>H_3</u>), 1.97 – 1.80 (2H, m, C**2**-<u>H_2</u>), 1.23 (9H, s, Boc (C<u>H_3</u>)$_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.7 (C=O), 154.1 (C**7**), 145.9 (Ts Ar<u>C</u>), 132.8 (C**4**), 131.0 (Ts Ar<u>C</u>), 129.6 (2 × Ts Ar<u>C</u>H), 129.5 (2 × Ts Ar<u>C</u>H), 129.3 (C**5**), 115.3 (C**6**), 83.6 (Boc <u>C</u>(CH$_3$)$_3$), 52.6 (C**1**), 31.9 (C**3**), 27.7 (C**2**), 27.6 (Boc (<u>C</u>H$_3$)$_3$), 21.7 (Ts, <u>C</u>H$_3$); HRMS (ESI$^+$) Calculated for $C_{21}H_{27}NNaO_6S$: 444.1451. Found [M+Na]$^+$: 444.1434.

1-Azaspiro[4.5]deca-6,9-dien-8-one trifluoroacetate (7a)

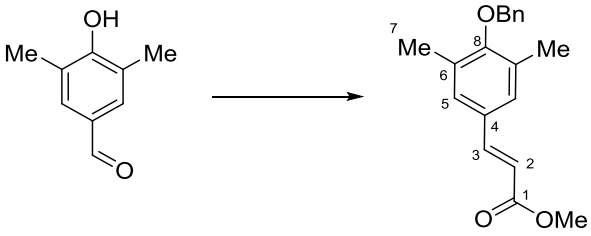


5a **7a**

General procedure E: *tert*-Butyl (3-(4-hydroxyphenyl)propyl)(tosyloxy)carbamate (**5a**) (60.7 mg, 0.14 mmol) and TFA (22 µL, 0.28 mmol) in TFE (1.4 mL) were stirred at r.t. for 24 h. Purification of the product by flash column chromatography (EtOAc) afforded **7a** (29.0 mg, 77 %) as a yellow solid; m.p.: 100 - 102 ^{o}C (EtOAc/hexane); R_f = 0.1 (5 % MeOH/CH_2Cl_2); ν_{max} / cm^{-1} (solid) 1651 (s), 1633 (s), 1426 (m), 1400 (m), 1192 (s), 1175 (s), 1130 (s); ^{1}H NMR (400 MHz, CD_3OD) δ 7.11 (2H, d, *J* = 10.3 Hz, C**5**-<u>H</u>), 6.43 (2H, d, *J* = 10.3 Hz, C**6**-<u>H</u>), 3.64 (2H, t, *J* = 7.4 Hz, C**1**-<u>H_2</u>), 2.42 - 2.34 (2H, m, C**2**-<u>H_2</u>), 2.30 - 2.25 (2H, m, C**3**-<u>H_2</u>). *The signals corresponding to the N<u>H_2</u> were not observed.* ^{13}C NMR (101 MHz, CD_3OD) δ 185.3 (C**7**), 144.5 (C**5**), 131.7 (C**6**), 64.5 (C**4**), 46.6 (C**1**), 37.8 (C**3**), 24.8 (C**2**). *The signals corresponding*

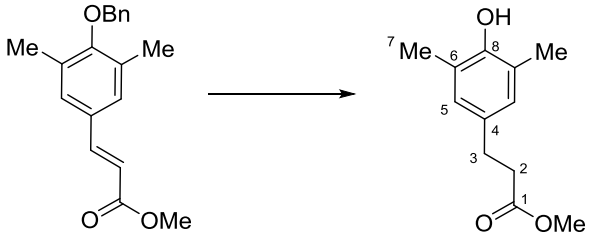
to the trifluoroacetate group could not be resolved due to their weak intensity. HRMS (ESI^+) Calculated for $C_9H_{12}NO$: 150.0913. Found $[M+H]^+$: 150.0908.

Methyl (*E*)-3-(4-(benzyloxy)-3,5-dimethylphenyl)acrylate



General procedure F: 4-(Benzyloxy)-3,5-dimethylbenzaldehyde (2.40 g, 10.0 mmol) and methyl 2-(triphenyl-phosphaneylidene) acetate (5.00 g, 15.0 mmol) in CH_2Cl_2 (15 mL) were employed. Purification by flash column chromatography (gradient, eluent 10 - 20 % EtOAc/hexane) afforded the title compound (2.85 g, 96 %) as a colorless oil; R_f = 0.6 (20 % EtOAc/hexane); ν_{max} / cm^{-1} (film) 1713 (s), 1632 (m), 1434 (m), 1265 (s), 1143 (s); ^1H NMR δ 7.63 (1H, d, *J* = 16.0 Hz, C**3**-H), 7.50 - 7.46 (2H, m, ArCH), 7.46 - 7.33 (3H, m, ArCH), 7.23 (2H, s, C**5**-H), 6.36 (1H, d, *J* = 16.0 Hz, C**2**-H), 4.83 (2H, s, OCH_2), 3.81 (3H, s, CH_3), 2.32 (6H, s, C**7**-H_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.7 (C**1**), 157.9 (C**8**), 144.8 (C**3**), 137.4 (PhC), 131.9 (C**6**), 130.2 (C**4**), 129.0 (C**5**), 128.7 (2 × PhCH), 128.2 (PhCH), 127.9 (2 × PhCH), 116.6 (C**2**), 74.2 (OCH_2), 51.7 (OCH_3), 16.6 (C**7**); HRMS (ESI^+) Calculated for $C_{19}H_{20}NaO_3$: 319.1305. Found $[M+Na]^+$: 319.1311.

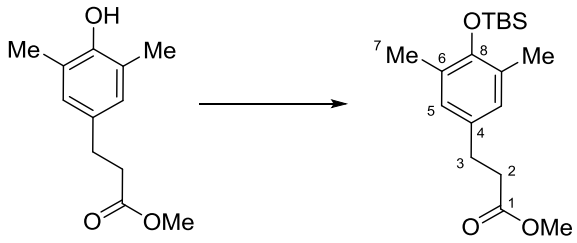
Methyl 3-(4-hydroxy-3,5-dimethylphenyl)propanoate[5]



General procedure G: Methyl (*E*)-3-(4-(benzyloxy)-3,5-dimethylphenyl)acrylate (2.37 g, 8.00 mmol) and 10 wt.% Pd/C (10 mol %) in MeOH (50 mL) were employed to afford the title compound (1.66 g, 99 %) as a colorless solid, which was used without further purification; m.p. 66 - 68 °C (EtOAc/hexane); R_f = 0.4 (20 % EtOAc/hexane); ν_{max} / cm^{-1} (solid) 3492 (s,

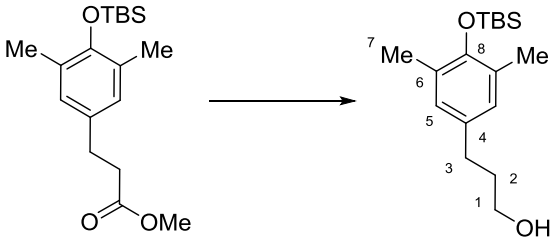
br), 2952 (m), 2928 (m), 1723 (s), 1277 (s), 1174 (s), 1151 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.81 (2H, s, C**5**-H), 4.55 (1H, br s, OH), 3.67 (3H, s, OCH_3), 2.82 (2H, t, *J* = 7.8 Hz, C**3**-H_2), 2.58 (2H, t, *J* = 7.8 Hz, C**2**-H_2), 2.22 (6H, s, C**7**-H_3); ^{13}C NMR (101 MHz, $CDCl_3$) 173.7, 150.7, 132.2, 128.5, 123.2, 51.7, 36.3, 30.3, 16.0, HRMS. (ESI^+) Calculated for $C_{12}H_{16}NaO_3$: 231.0992. Found $[M+Na]^+$: 231.1002. *The title compound has been described only in a patent.*

Methyl 3-(4-((*tert*-butyldimethylsilyl)oxy)-3,5-dimethylphenyl)propanoate



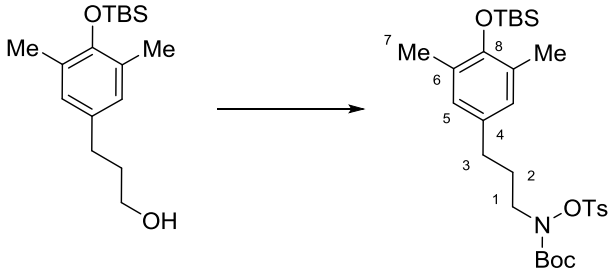
To a solution of methyl 3-(4-hydroxy-3,5-dimethylphenyl)propanoate (1.33 g, 6.00 mmol) in CH_2Cl_2 (10 mL) and DMF (12 mL) was added *tert*-butyldimethylsilyl chloride (1.8 g, 12.0 mmol) and imidazole (0.82 g, 12.0 mmol) at 0 ^{o}C. The reaction was stirred at r.t. overnight and quenched with H_2O (50 mL) and the organic phase extracted with CH_2Cl_2 (3 × 15 mL), washed with brine (15 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by flash column chromatography (10 % EtOAc/hexane) afforded the title compound (1.22 g, 63 %) as a colorless oil; R_f = 0.6 (25 % EtOAc/hexane); ν_{max} / cm^{-1} (film) 2953 (m), 2930 (m), 1740 (s), 1484 (m), 1473 (m), 1253 (s), 1228 (s), 1153 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.79 (2H, s, C**5**-H), 3.67 (3H, s, OCH_3), 2.81 (2H, t, *J* = 7.8 Hz, C**3**-H_2), 2.58 (2H, t, *J* = 7.8 Hz, C**2**-H_2), 2.18 (6H, s, C**7**-H_3), 1.03 (9H, s, TBS (CH_3)$_3$), 0.18 (6H, s, TBS (CH_3)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.7 (C**1**), 150.6 (C**8**), 133.1 (C**4**), 128.6 (C**5**), 128.6 (C**6**), 51.7 (OCH_3), 36.2 (C**2**), 30.3 (C**3**), 26.3 (TBS (CH_3)$_3$), 18.9 (TBS C(CH_3)$_3$), 18.0 (C**7**), -2.8 (TBS Si(CH_3)$_2$); HRMS (ESI^+) Calculated for $C_{18}H_{30}NaO_3Si$: 345.1856. Found $[M+Na]^+$: 345.1870.

3-(4-((*tert*-Butyldimethylsilyl)oxy)-3,5-dimethylphenyl)propan-1-ol[6]



General procedure B: Methyl 3-(4-((*tert*-butyldimethylsilyl)oxy)-3,5-dimethylphenyl)propanoate (0.96 mg, 3.0 mmol) and 2.0 eq. $LiAlH_4$ (1 M in THF) in anhydrous Et_2O were employed. The crude product was filtered through a plug of silica and washed with EtOAc to afford the title compound (0.69 mg, 80 %) as a pale yellow oil; R_f = 0.2 (25 % EtOAc/hexane); ν_{max} / cm^{-1} (film) 3345 (br m), 2929 (m), 2858 (m), 1483 (s), 1472 (s), 1252 (s), 1227 (s), 1152 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.79 (2H, s), 3.66 (2H, t, *J* = 6.4 Hz), 2.57 (2H, t, *J* = 7.5 Hz), 2.18 (6H, s), 1.89-1.81 (2H, m), 1.29 (1H, br s), 1.03 (9H, s), 0.18 (6H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.1, 134.2, 128.6, 128.3, 62.5, 34.3, 31.2, 26.1, 18.7, 17.8, -3.0. *Spectroscopic properties were consistent with the data available in the literature.* [6]

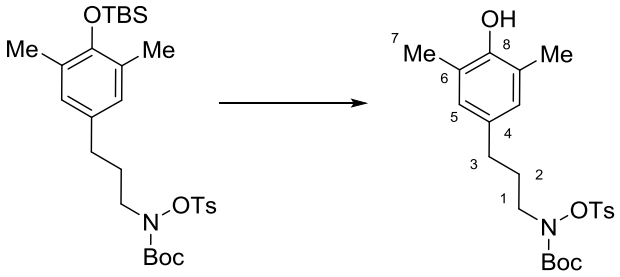
***tert*-Butyl (3-(4-((*tert*-butyldimethylsilyl)oxy)-3,5-dimethylphenyl)propyl)(tosyloxy) carbamate**



General procedure C: 3-(4-((*tert*-Butyldimethylsilyl)oxy)-3,5-dimethylphenyl)propan-1-ol (0.53 g, 1.80 mmol), PPh_3 (0.58 g, 2.20 mmol), DIAD (0.43 mL, 2.20 mmol) and TsONHBoc (0.63 g, 2.20 mmol) in anhydrous THF (8 mL) were employed. Purification by flash column chromatography (10 % EtOAc/hexane) afforded the title compound (0.88 g, 87 %) as a colorless oil; R_f = 0.55 (20 % EtOAc/hexane); ν_{max} / cm^{-1} (film) 2955 (m), 2930 (m), 1722 (s), 1473 (m), 1483 (m), 1383 (s), 1369 (s), 1230 (s), 1191 (s), 1179 (s), 1154 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (2H, d, *J* = 8.3 Hz, Ts ArC<u>H</u>), 7.32 (2H, d, *J* = 8.3 Hz, Ts ArC<u>H</u>), 6.75 (2H, s, C**5**-<u>H</u>), 3.61 (2H, app. br s, C**1**-<u>H_2</u>), 2.46-2.42 (5H, m, overlapping C**3**-<u>H_2</u> and Ts C<u>H_3</u>),

2.18 (6H, s, C**7**-H$_3$) 1.93-1.81 (2H, m, C**2**-H$_2$), 1.21 (9H, s, Boc (CH$_3$)$_3$), 1.03 (9H, s, TBS (CH$_3$)$_3$), 0.17 (6H, s, TBS Si(CH$_3$)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.6 (Boc C=O), 150.4 (C**8**), 145.7 (Ts ArC), 133.7 (C**4**), 131.4 (Ts ArC), 129.8 (2 × Ts ArCH), 129.6 (2 × Ts ArCH), 128.7 (C**5**), 128.5 (C**6**), 83.2 (Boc C(CH$_3$)$_3$), 52.9 (C**1**), 32.1 (C**3**), 27.8 (C**2**), 27.7 (Boc (CH$_3$)$_3$), 26.3 (TBS (CH$_3$)$_3$), 21.9 (Ts CH$_3$), 18.9 (TBS C(CH$_3$)$_3$), 18.0 (C**7**), -2.8 (TBS (CH$_3$)$_2$); HRMS (ESI$^+$) Calculated for $C_{29}H_{45}NNaO_6SSi$: 586.2629. Found $[M+Na]^+$: 586.2648.

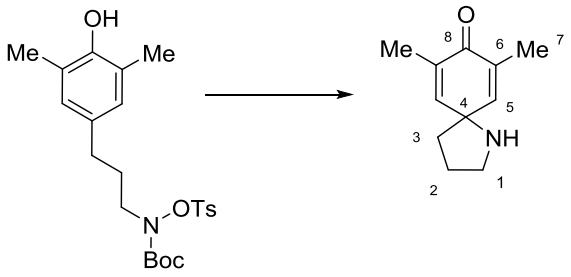
***tert*-Butyl (3-(4-hydroxy-3,5-dimethylphenyl)propyl)(tosyloxy)carbamate (5b)**



5b

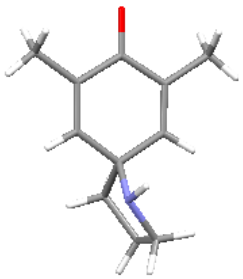
General procedure D: *tert*-Butyl (3-(4-((*tert*-butyldimethylsilyl)oxy)-3,5-dimethylphenyl)propyl) (tosyloxy)carbamate (0.45 g, 0.80 mmol) and 1:1 TBAF/HOAc solution (0.1 M in THF, 0.88 mmol) in THF (16 mL) were employed. Purification by flash column chromatography (gradient, eluent 20 - 33 % EtOAc/hexane) afforded **5b** (0.31 g, 87 %) as a colorless, viscous oil; R_f = 0.3 (20 % EtOAc/hexane); ν_{max} / cm^{-1} (film) 3530 (br m), 2979 (m), 2930 (m), 1721 (s), 1597 (m), 1489 (m), 1370 (s), 1192 (s), 1177 (s), 1152 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (2H, d, *J* = 8.3 Hz, Ts ArCH), 7.32 (2H, d, *J* = 8.3 Hz, Ts ArCH), 6.77 (2H, s, C**5**-H), 4.49 (1H, s, OH), 3.62 (2H, app. br s, C**1**-H$_2$), 2.44 (5H, m, overlapping C**3**-H$_2$ and Ts CH$_3$), 2.21 (6H, s, C**7**-H$_3$), 1.93-1.85 (2H, m, C**2**-H$_2$), 1.20 (9H, s, Boc (CH$_3$)$_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.6 (Boc C=O), 150.5 (C**8**), 145.8 (Ts ArC), 132.8 (C**4**), 131.4 (Ts ArC), 129.8 (2 × Ts ArCH), 129.6 (2 × Ts ArCH), 128.5 (C**5**), 123.0 (C**6**), 83.3 (Boc C(CH$_3$)$_3$), 52.8 (C**1**), 32.1 (C**3**), 27.9 (C**2**), 27.7 (Boc (CH$_3$)$_3$), 21.8 (Ts CH$_3$), 16.0 (C**7**); HRMS (ESI$^+$) Calculated for $C_{23}H_{31}NNaO_6S$: 472.1764. Found $[M+Na]^+$: 472.1767.

7,9-Dimethyl-1-azaspiro[4.5]deca-6,9-dien-8-one (7b)

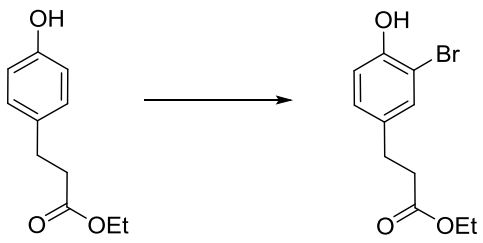


5b **7b**

General procedure E: *tert*-Butyl (3-(4-hydroxy-3,5-dimethylphenyl)propyl)(tosyloxy) carbamate (**5b**) (89.8 mg, 0.20 mmol) and TFA (31.0 μL, 0.40 mmol) in TFE (2 mL) were employed. After stirring at r.t. for 22 h, purification by flash column chromatography (EtOAc) afforded **7b** (30.0 mg, 85 %) as a pale yellow/orange solid; m.p.: 110 - 113 ºC (EtOAc/hexane); R_f = 0.1 (EtOAc); ν_{max} / cm^{-1} (film) 3318 (m), 2970 (m), 2946 (m), 2917 (m), 2882 (m), 1664 (s), 1623 (s), 1369 (m), 1222 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.60 (2H, s, C**5**-H), 3.19 (2H, t, *J* = 6.9 Hz, C**1**-H_2), 2.04-1.96 (2H, m, C**2**-H_2), 1.87-1.84 (9H, m, overlapping C**3**-H_2, C**7**-H_3 and NH); ^{13}C NMR (101 MHz, $CDCl_3$) δ 187.2 (C**8**), 147.7 (C**5**), 132.7 (C**6**), 60.4 (C**4**), 46.1 (C**1**), 36.7 (C**3**), 25.5 (C**2**), 16.0 (C**7**); HRMS (ESI^+) Calculated for $C_{11}H_{16}NO$: 178.1226. Found $[M+H]^+$: 178.1228.



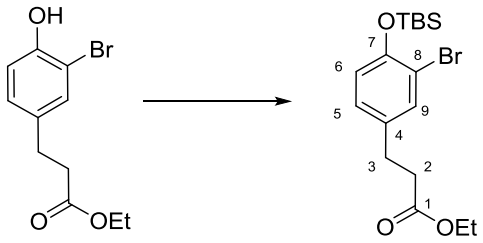
Ethyl 3-(3-bromo-4-hydroxyphenyl)propanoate[7]



A solution of bromine (0.25 mL, 4.75 mmol) in acetic acid (20 mL) was slowly added to a stirring solution of ethyl 3-(4-hydroxyphenyl)propionate (1.84 g, 9.50 mmol) at r.t. The

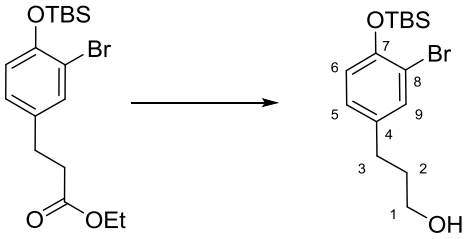
reaction mixture was stirred for 6 h then diluted with EtOAc (80 mL) and washed with brine (2 × 30 mL). The organic extracts were dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. Purification by flash column chromatography (5 % EtOAc/PhMe) afforded the title compound (1.14 g, 44 %) as a pale yellow solid; R_f = 0.3 (5 % EtOAc/PhMe); ν_{max} / cm^{-1} (solid) 3357 (br m), 2977 (m), 2936 (m), 1727 (s), 1704 (s), 1496 (s), 1289 (s), 1254 (s), 1180 (s), 1156 (s), 1039 (s); ^{1}H NMR (400 MHz, $CDCl_3$) 7.29 (1H, d, *J* = 2.0 Hz), 7.03 (1H, dd, *J* = 8.2, 2.0 Hz), 6.91 (1H, d, *J* = 8.2 Hz), 4.11 (2H, q, *J* = 7.2 Hz), 2.85 (2H, t, *J* = 8.5 Hz), 2.56 (2H, t, *J* = 7.6 Hz), 1.22 (3H, t, *J* = 7.2 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.7, 150.7, 134.2, 131.6, 129.1, 116.0, 110.0, 60.5, 36.0, 29.8, 14.2. *Spectroscopic properties are consistent the data available in the literature.*[7]

Ethyl 3-(3-bromo-4-((*tert*-butyldimethylsilyl)oxy)phenyl)propanoate



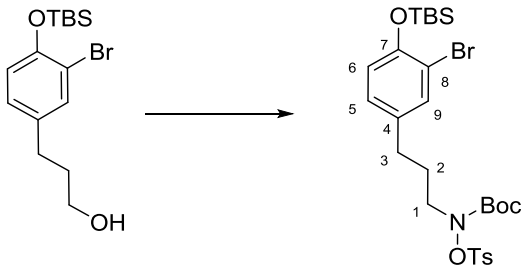
To a solution of ethyl 3-(3-bromo-4-hydroxyphenyl)propanoate (1.08 g, 3.95 mmol) in DMF (5 mL) was added *tert*-butyldimethylsilyl chloride (0.71 g, 4.74 mmol) and imidazole (0.67 g, 9.88 mmol) and the reaction was stirred at r.t. overnight. To the reaction was added water (25 mL) and the organic phase extracted with CH_2Cl_2 (2 x 20 mL). The combined organic extracts were washed with brine (20 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by flash column chromatography (5% EtOAc/hexane) afforded the title compound (1.43 g, 93 %) as a colorless oil; R_f = 0.6 (5 % EtOAc/hexane); ν_{max} / cm^{-1} (film) 2956 (m), 2930 (m), 1734 (s), 1493 (s), 1287 (s), 1253 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (1H, d, *J* = 2.2 Hz, C**9**-H), 6.98 (1H, dd, *J* = 8.4, 2.2 Hz, C**5**-H), 6.77 (1H, d, *J* = 8.4 Hz, C**6**-H), 4.11 (2H, q, *J* = 7.1 Hz, OCH_2), 2.84 (2H, t, *J* = 7.7 Hz, C**3**-H_2), 2.56 (2H, t, *J* = 7.7 Hz, C**2**-H_2), 1.22 (3H, t, *J* = 7.1 Hz, CH_2CH_3), 1.03 (9H, s, TBS (CH_3)$_3$), 0.22 (6H, TBS (CH_3)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.8 (C**1**), 151.1 (C**7**), 134.9 (C**4**), 133.2 (C**9**), 128.2 (C**5**), 120.2 (C**6**), 115.2 (C**8**), 60.6 (OCH_2CH_3), 36.1 (C**2**), 29.9 (C**3**), 25.9 (TBS (CH_3)$_3$), 18.5 (TBS Si$C(CH_3)_3$), 14.4 (OCH_2CH_3), -4.11 (TBS Si(CH_3)$_2$); HRMS (ESI^+) Calculated for $C_{17}H_{27}{}^{79}BrNaO_3Si$: 409.0805. Found $[M+Na]^+$: 409.0816.

3-(3-Bromo-4-((*tert*-butyldimethylsilyl)oxy)phenyl)propan-1-ol



To a solution of ethyl 3-(3-bromo-4-((*tert*-butyldimethylsilyl)oxy)phenyl)propanoate (1.03 g, 2.66 mmol) in anhydrous THF (15 mL) at -15 ^{o}C was added 0.75 eq. $LiAlH_4$ (1M in THF) and the reaction was stirred at the same temperature for 25 min. Then to the reaction mixture was added water (0.5 mL), aq. 1 M NaOH (0.2 mL) and water (1 mL). The reaction mixture was warmed to r.t., filtered through Celite® and washed with CH_2Cl_2. The filtrate was dried over Na_2SO_4, filtered and concentrated *in vacuo*. Purification by flash column chromatography (20 % EtOAc/hexane) afforded the title compound (0.80 g, 87 %) as a colorless oil; R_f = 0.2 (20 % EtOAc/hexane); ν_{max} / cm^{-1} (film) 3327 (br m), 2930 (m), 2858 (m), 1492 (s), 1280 (s), 1253 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (1H, d, *J* = 2.2 Hz, C**9**-H), 6.97 (1H, dd, *J* = 8.2, 2.2 Hz, C**5**-H), 6.77 (1H, dd, *J* = 8.2, 0.8 Hz, C**6**-H), 3.63 (2H, t, *J* = 6.5 Hz, C**1**-H_2), 2.60 (2H, t, *J* = 7.5 Hz, C**3**-H_2), 1.87-1.80 (2H, m, C**2**-H_2), 1.51 (1H, br s, OH), 1.03 (9H, s, TBS (CH_3)$_3$), 0.22 (6H, s, TBS (CH_3)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.7 (C**7**), 136.1 (C**4**), 133.2 (C**9**), 128.3 (C**5**), 120.2 (C**6**), 115.2 (C**8**), 62.1 (C**1**), 34.2 (C**2**), 31.0 (C**3**), 25.9 (TBS (CH_3)$_3$), 18.5 (TBS $C(CH_3)_3$), -4.1 (TBS Si(CH_3)$_2$); HRMS (ESI$^+$) Calculated for $C_{15}H_{25}{}^{79}BrNaO_2Si$: 367.0699. Found $[M+Na]^+$: 367.0701.

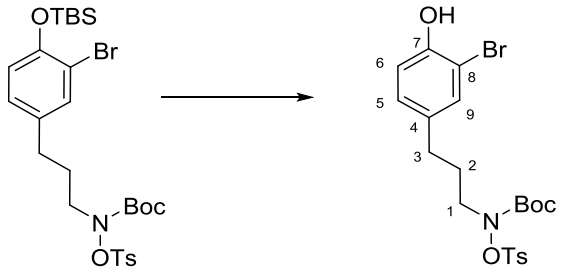
***tert*-Butyl (3-(3-bromo-4-((*tert*-butyldimethylsilyl)oxy)phenyl)propyl) (tosyloxy) carbamate**



General procedure C: 3-(3-Bromo-4-((*tert*-butyldimethylsilyl)oxy)phenyl)propan-1-ol (0.69 g, 2.00 mmol), PPh_3 (0.63 g, 2.40 mmol), DIAD (0.47 mL, 2.40 mmol) and TsONHBoc (0.69

g, 2.40 mmol) in anhydrous THF were employed. Purification by flash column chromatography (gradient eluent 5 % - 10 % EtOAc/hexane) afforded the title compound (1.12 g, 91 %) as a colorless oil; R_f = 0.6 (20 % EtOAc/hexane); ν_{max} / cm^{-1} (film) 2955 (m), 2930 (m), 2858 (m), 1720 (s), 1493 (s), 1381 (s), 1368 (s), 1288 (s), 1254 (s), 1178 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (2H, d, *J* = 8.2 Hz, Ts ArC<u>H</u>), 7.32 (2H, d, *J* = 8.0 Hz, Ts ArC<u>H</u>), 7.29 (1H, d, *J* = 2.1 Hz, C**9**-<u>H</u>), 6.94 (1H, dd, *J* = 8.3, 2.2 Hz, C**5**-<u>H</u>), 6.77 (1H, d, *J* = 8.6 Hz, C**6**-<u>H</u>), 3.58 (2H, app. br s, C**1**-<u>H_2</u>), 2.49 (2H, t, *J* = 7.8 Hz, C**3**-<u>H_2</u>), 2.44 (3H, s, Ts C<u>H_3</u>), 1.95-1.82 (2H, m, C**2**-<u>H_2</u>), 1.22 (9H, s, Boc (C<u>H_3</u>)$_3$), 1.03 (9H, s, TBS (C<u>H_3</u>)$_3$), 0.23 (6H, s, Si(CH_3)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.6 (C=O), 150.9 (C**7**), 145.8 (Ts Ar<u>C</u>), 135.4 (C**4**), 133.1 (C**9**), 131.4 (Ts Ar<u>C</u>), 129.8 (2 × Ts Ar<u>C</u>H), 129.7 (2 × Ts Ar<u>C</u>H), 128.2 (C**5**), 120.2 (C**6**), 115.2 (C**8**), 83.4 (Boc <u>C</u>(CH_3)$_3$), 52.6 (C**1**), 31.8 (C**3**), 27.8 (Boc (C<u>H_3</u>)$_3$), 27.5 (C**2**), 25.9 (TBS (<u>C</u>H_3)$_3$), 21.8 (Ts <u>C</u>H_3), 18.5 (TBS Si<u>C</u>(CH_3)$_3$), -4.1 (TBS Si(<u>C</u>H_3)$_2$); HRMS (ESI^+) Calculated for $C_{27}H_{40}{}^{79}BrNNaO_6SSi$: 636.1421. Found $[M+Na]^+$: 636.1422.

***tert*-Butyl (3-(3-bromo-4-hydroxyphenyl)propyl)(tosyloxy)carbamate (5c)**

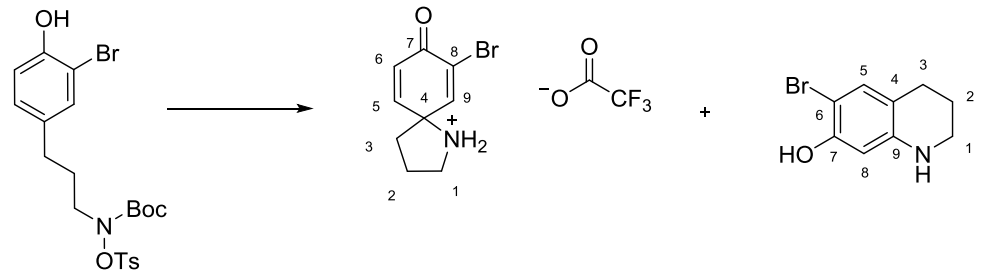


5c

General procedure D: *tert*-Butyl (3-(3-bromo-4-((*tert*-butyldimethylsilyl)oxy)phenyl)propyl) (tosyloxy)carbamate (0.61 g, 1.00 mmol) and 1:1 solution of TBAF/AcOH (0.1 M in THF, 1.00 mmol) in THF (20 mL) were employed. Purification by flash column chromatography (20 % EtOAc/hexane) afforded **5c** (0.48 g, 96 %) as a colorless solid; m.p.: 93 - 95 ºC (EtOAc/hexane); R_f = 0.25 (20 % EtOAc/hexane); ν_{max} / cm^{-1} (solid) 3416 (br s), 2945 (m), 1682 (s), 1371 (s), 1361 (s), 1180 (s), 1158 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (2H, d, *J* = 8.3 Hz, Ts ArC<u>H</u>), 7.32 (2H, d, *J* = 8.1 Hz, Ts ArC<u>H</u>), 7.25 (1H, d, *J* = 2.2 Hz, C**9**-<u>H</u>), 7.00 (1H, dd, *J* = 8.3, 2.1 Hz, C**5**-<u>H</u>), 6.91 (1H, d, *J* = 8.3 Hz, C**6**-<u>H</u>), 5.43 (1H, s, O<u>H</u>), 3.59 (2H, app. br s, C**1**-<u>H_2</u>), 2.50 (2H, t, *J* = 7.8 Hz, C**3**-<u>H_2</u>), 2.44 (3H, s, Ts C<u>H_3</u>), 1.91-1.87 (2H, m, C**2**-<u>H_2</u>), 1.21 (9H, s, Boc (C<u>H_3</u>)$_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.6 (C=O), 150.6 (C**7**), 145.9

(Ts Ar<u>C</u>), 134.9 (C**4**), 131.6 (C**9**), 131.3 (Ts Ar<u>C</u>), 129.8 (2 × Ts Ar<u>C</u>H), 129.7 (2 × Ts Ar<u>C</u>H), 129.2 (C**5**), 116.1 (C**6**), 110.1 (C**8**), 83.5 (Boc <u>C</u>(CH_3)$_3$), 52.5 (C**1**), 31.7 (C**3**), 27.8 (Boc (<u>C</u>H_3)$_3$), 27.6 (C**2**), 21.8 (Ts <u>C</u>H_3); HRMS (ESI$^+$) Calculated for $C_{21}H_{26}{}^{79}BrNO_6S$: 522.0556. Found $[M+Na]^+$: 522.0555.

7-bromo-1-azaspiro[4.5]deca-6,9-dien-8-one trifluoroacetate (7c) ***and*** **6-Bromo-1,2,3,4-tetrahydroquinolin-7-ol (8c)**



5c **7c** **8c**

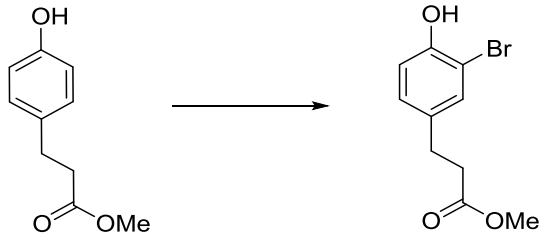
General procedure E: *tert*-Butyl (3-(3-bromo-4-hydroxyphenyl)propyl)(tosyloxy)carbamate (**5c**) (75.06 mg, 0.15 mmol) and TFA (22.9 μL, 0.30 mmol) in TFE (1.5 mL) were employed. After stirring at r.t. for 45 h, purification by flash column chromatography (EtOAc) afforded the title compounds **7c** (22.0 mg, 43 %) as a red/brown oil and **8c** (8.8 mg, 19 %) as a brown oil.

Data for **7c**; R_f = 0.1 (EtOAc); ν_{max} / cm^{-1} (film, $CDCl_3$) 2924 (m), 1675 (s), 1407 (w), 1200 (s), 1134 (m), 1066 (m); ^{1}H NMR (400 MHz, CD_3OD) δ 7.63 (1H, d, *J* = 3.0 Hz, C**9**-<u>H</u>), 7.14 (1H, dd, *J* = 10.0, 3.0 Hz, C**5**-<u>H</u>), 6.55 (1H, d, *J* = 10.1 Hz, C**6**-<u>H</u>), 3.64 (2H, t, *J* = 6.9 Hz, C**1**-<u>H</u>$_2$), 2.41-2.30 (4H, m, C**2**-<u>H</u>$_2$, C**3**-<u>H</u>$_2$). *The signals corresponding to the N<u>H</u>$_2$ were not observed.* ^{13}C NMR (101 MHz, CD_3OD) δ 178.1 (C**7**), 144.7 (C**9**), 144.6 (C**5**), 130.3 (C**6**), 128.3 (C**8**), 66.9 (C**4**), 46.7 (C**1**), 37.4 (C**3**), 24.8 (C**2**). *The signals corresponding to the trifluoroacetate group could not be resolved due to their weak intensity*. HRMS (ESI$^+$) Calculated for $C_9H_{11}{}^{79}BrNO$: 228.0019. Found $[M]^+$: 228.0019.

Data for **8c**; R_f = 0.7 (EtOAc); ν_{max} / cm^{-1} (film) 3389 (m), 3197 (m), 2957 (m), 2918 (m), 2850 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.97 (1H, s, C**5**-<u>H</u>), 6.16 (1H, s, C**8**-<u>H</u>), 3.27-3.24 (2H, m, C**1**-<u>H</u>$_2$), 2.66 (2H, t, *J* = 6.4 Hz, C**3**-<u>H</u>$_2$), 1.91-1.85 (2H, m, C**2**-<u>H</u>$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.8 (C**7**), 145.1 (C**9**), 131.7 (C**5**), 115.8 (C**4**), 100.8 (C**8**), 96.6 (C**6**), 41.7 (C**1**),

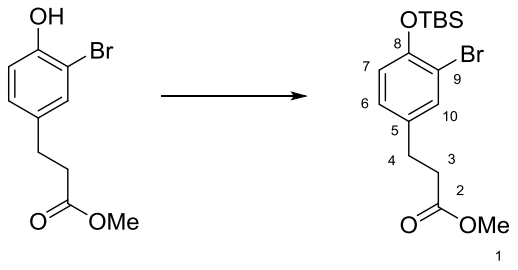
26.1 (C**3**), 21.9 (C**2**). HRMS (ESI$^+$) Calculated for $C_9H_{11}{}^{79}BrNO$: 228.0018. Found $[M]^+$: 228.0029.

Methyl 3-(3-bromo-4-hydroxyphenyl)propanoate[8]



To a solution of methyl 3-(4-hydroxyphenyl)propanoate (4.50 g, 25.0 mmol) in AcOH (20 mL) was slowly added a solution of Br_2 (1.3 mL, 25.0 mmol) in AcOH (15 mL). The reaction was stirred at r.t. until completion by TLC analysis. The reaction was diluted with EtOAc (20 mL) and washed with brine (20 mL), dried over Na_2SO_4, filtered, and the solvent removed *in vacuo*. Purification by flash column chromatography (20 % EtOAc/hexane) afforded the title compound (2.98 g, 46 %) as a colorless solid; R_f = 0.2 (20% EtOAc/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (1H, d, *J* = 2.1 Hz), 7.05 (1H, dd, *J* = 8.3, 2.0 Hz), 6.93 (1H, d, *J* = 8.3 Hz), 3.67 (3H, s), 2.86 (2H, t, *J* = 7.7 Hz), 2.59 (2H, dd, *J* = 8.6, 6.7 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.2, 150.8, 134.3, 131.7, 129.2, 116.1, 110.1, 51.8, 35.8, 29.7. *Spectroscopic properties were consistent with the data available in the literature.*[8]

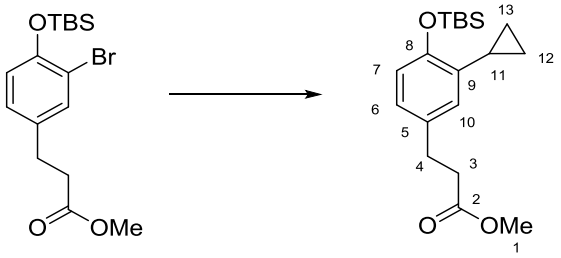
Methyl 3-(3-bromo-4-((*tert*-butyldimethylsilyl)oxy)phenyl)propanoate



To a solution of methyl 3-(3-bromo-4-hydroxyphenyl)propanoate (2.94 g, 11.3 mmol) in DMF (5 mL) was added *tert*-butyldimethylsilyl chloride (2.05 g, 13.6 mmol) and imidazole (1.93 g, 28.4 mmol) and the reaction was stirred at r.t. overnight. To the reaction was added water (25

mL) and the organic phase was extracted with CH_2Cl_2 (2 × 20 mL). The combined organic phases were washed with brine (20 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by flash column chromatography (20 % EtOAc/hexane) afforded the title compound (3.53 g, 84 %) as a colorless oil; R_f = 0.4 (20 % EtOAc/hexane); ν_{max} / cm^{-1} (film) 2952 (m), 2930 (m), 2858 (m), 1738 (s), 1492 (s), 1253 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (1H, d, *J* = 2.2 Hz, C**10**-H), 7.04-6.93 (1H, m, C**6**-H), 6.78 (1H, d, *J* = 8.2 Hz, C**7**-H), 3.67 (3H, s, C**1**-H_3), 2.85 (2H, t, *J* = 7.8 Hz, C**4**-H_2), 2.58 (2H, t, *J* = 7.8 Hz, C**3**-H_2), 1.03 (9H, s, TBS (CH_3)$_3$), 0.23 (6H, s, TBS Si(CH_3)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3 (C**2**), 151.1 (C**8**), 134.8 (C**5**), 133.2 (C**10**), 128.2 (C**6**), 120.2 (C**7**), 115.3 (C**9**), 51.8 (C**1**), 35.8 (C**4**), 29.9 (C**3**), 25.9 (TBS (CH_3)$_3$), 18.5 (TBS C(CH_3)$_3$), -4.1 (TBS Si(CH_3)$_2$). HRMS (ESI$^+$) Calculated for $C_{16}H_{25}{}^{79}BrNaO_3Si$: 395.0648. Found $[M+Na]^+$: 395.0647.

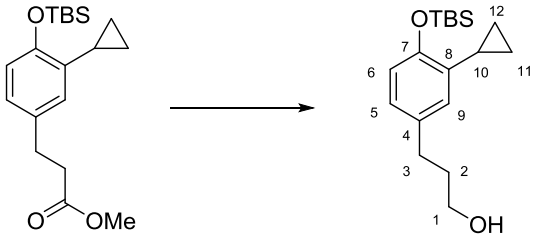
Methyl 3-(4-((*tert*-butyldimethylsilyl)oxy)-3-cyclopropylphenyl)propanoate



Methyl 3-(3-bromo-4-((*tert*-butyldimethylsilyl)oxy)phenyl)propanoate (1.12 g, 3.00 mmol), cyclopropylboronic acid (0.77 g, 9.00 mmol), K_3PO_4 (3.82 g, 18.0 mmol) and tetrakis(triphenylphosphine)palladium (0) ($Pd(PPh_3)_4$) (346 mg, 0.30 mmol) in 20:1 toluene/H_2O (0.1 M) were heated at 95 ^{o}C overnight, under an atmosphere of N_2, and monitored by GC-MS. Upon completion, the reaction was cooled to r.t. and filtered through Celite® washing with EtOAc. The crude reaction mixture was then washed with water and the organic layer was dried over Na_2SO_4, filtered and concentrated *in vacuo*. Purification by flash column chromatography (5 % EtOAc/hexane) afforded the title compound (0.81 g, 80 %) as a pale yellow oil; R_f = 0.5 (20 % EtOAc/hexane); ν_{max} / cm^{-1} (film) 2953 (m), 2930 (m), 2897 (m), 2858 (m), 1739 (s), 1498 (s), 1255 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.85 (1H, dd, *J* = 8.2, 2.3 Hz, C**6**-H), 6.70 (1H, d, *J* = 8.2 Hz, C**7**-H), 6.62 (1H, d, *J* = 2.2 Hz, C**10**-H), 3.67 (3H, s, C**1**-H_3), 2.84 (2H, t, *J* = 8.0 Hz, C**4**-H_2), 2.57 (2H, t, *J* = 8.0 Hz, C**3**-H_2), 2.13 (1H, tt, *J* = 8.7, 5.4 Hz, C**11**-H), 1.03, (9H, s, TBS (CH_3)$_3$), 0.93 - 0.87 (2H, m, C**12**/**13**-H_2), 0.64 - 0.60 (2H, m, C**12**/C**13**-H_2), 0.23 (6H, s, TBS Si(CH_3)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.6 (C**2**), 152.9

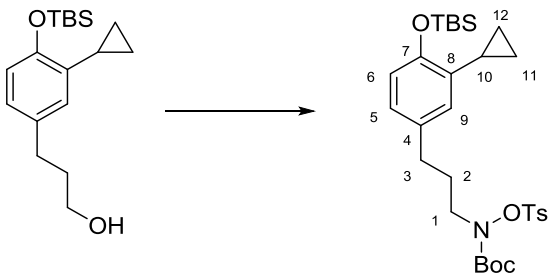
(C**8**), 134.2 (C**9**) , 133.2 (C**5**), 125.7 (C**6**), 124.8 (C**10**), 118.7 (C**7**), 51.7 (C**1**), 36.2 (C**3**), 30.6 (C**4**), 25.9 (TBS ($\underline{C}H_3)_3$), 18.4 (TBS $\underline{C}(CH_3)_3$), 10.1 (C**11**), 8.2 (C**12**.C**13**), -4.1 (TBS Si($\underline{C}H_3)_2$). HRMS (ESI$^+$) Calculated for $C_{19}H_{30}NaO_3Si$: 357.1856. Found [M+Na]$^+$: 357.1862.

3-(4-((*tert*-Butyldimethylsilyl)oxy)-3-cyclopropylphenyl)propan-1-ol



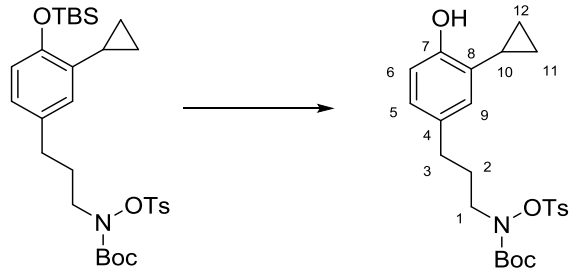
General procedure B: Methyl 3-(4-((*tert*-butyldimethylsilyl)oxy)-3-cyclopropylphenyl) propanoate (0.67 g, 2.00 mmol) and 2.0 eq. $LiAlH_4$ (1 M in THF) in anhydrous Et_2O were employed. Purification by flash column chromatography (20 % EtOAc/hexane) afforded the title compound (0.48 g, 78 %) as a colorless oil; R_f = 0.2 (20 % EtOAc/hexane); ν_{max} / cm^{-1} (film) 3334 (m, br), 2953 (m), 2929 (m), 2885 (m), 2857 (m), 1496 (s), 1254 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.84 (1H, dd, *J* = 8.1, 2.3 Hz, C**5**-$\underline{H}$), 6.70 (1H, d, *J* = 8.1 Hz, C**6**-$\underline{H}$), 6.61 (1H, d, *J* = 2.2 Hz, C**9**-$\underline{H}$), 3.65 (2H, t, *J* = 6.4 Hz, C**1**-$\underline{H}_2$), 2.59 (2H, dd, *J* = 8.6, 6.8 Hz, C**3**-$\underline{H}_2$), 2.12 (1H, tt, *J* = 8.7, 5.4 Hz, C**10**-$\underline{H}$), 1.88 - 1.79 (2H, m, C**2**-$\underline{H}_2$), 1.40 (1H, br s, O$\underline{H}$), 1.03 (9H, s, TBS ($C\underline{H}_3)_3$), 0.92 - 0.88 (2H, m, C**11**/C1**2**-$\underline{H}_2$), 0.64 - 0.60 (2H, m, C**11**/C**12**-$\underline{H}_2$), 0.23 (6H, s, TBS Si($C\underline{H}_3)_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.6 (C**7**), 134.4 (C**4**), 134.1 (C**8**), 125.8 (C**5**), 124.9 (C**9**), 118.6 (C**6**), 62.5 (C**1**), 34.6 (C**2**), 31.6 (C**3**), 26.0 (TBS ($\underline{C}H_3)_3$), 18.4 (TBS $\underline{C}(CH_3)_3$), 10.1 (C**10**), 8.2 (C**11**,C**12**), -4.1 (TBS Si($\underline{C}H_3)_2$). HRMS (ESI$^+$) Calculated for $C_{18}H_{30}NaO_2Si$: 329.1907. Found [M+Na]$^+$: 329.1940.

***tert*-Butyl (3-(4-((*tert*-butyldimethylsilyl)oxy)-3-cyclopropylphenyl)propyl)(tosyloxy) carbamate**



General procedure C: 3-(4-((*tert*-Butyldimethylsilyl)oxy)-3-cyclopropylphenyl)propan-1-ol (0.43 g, 1.40 mmol), PPh_3 (0.44 g, 1.68 mmol), DIAD (0.33 mL, 1.68 mmol) and TsONHBoc (0.48 g, 1.68 mmol) in anhydrous THF (6 mL) were employed. Purification by flash column chromatography (5 % EtOAc/hexane) afforded the title compound (0.77 g, 96 %) as a colorless solid; R_f = 0.5 (20 % EtOAc/hexane); ν_{max} / cm^{-1} (solid) 2949 (m), 2928 (m), 2883 (m), 2857 (m), 1712 (s), 1504 (m); ^1H NMR (400 MHz, $CDCl_3$) δ 7.84 (2H, d, *J* = 8.3 Hz, Ts ArC<u>H</u>), 7.33 (2H, d, *J* = 8.1 H, Ts ArC<u>H</u>), 6.80 (1H, dd, *J* = 8.1, 2.1 Hz, C**5**-<u>H</u>), 6.68 (1H, d, *J* = 8.2 Hz, C**6**-<u>H</u>), 6.57 (1H, d, *J* = 2.2 Hz, C**9**-<u>H</u>), 3.60 (2H, app. br s, C**1**-<u>H_2</u>), 2.49 - 2.44 (5H, m, C**3**-<u>H_2</u> and Ts C<u>H_3</u>), 2.15 - 2.08 (1H, m, C**10**-<u>H</u>), 1.94 - 1.83 (2H, m, C**2**-<u>H_2</u>), 1.22 (9H, s, Boc (C<u>H_3</u>)$_3$), 1.03 (9H, s, TBS (C<u>H_3</u>)$_3$), 0.92 - 0.86 (2H, m, C**11**/C**12**-<u>H_2</u>), 0.64 - 0.60 (2H, m, C**11**/C**12**-<u>H_2</u>), 0.22 (6H, s, TBS Si(C<u>H_3</u>)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.6 (C=O), 152.7 (C**7**), 145.7 (Ts Ar<u>C</u>), 134.1 (C**8**), 133.7 (C**4**), 131.4 (Ts Ar<u>C</u>), 129.8 (2 × Ts <u>CH</u>), 129.6 (2 × Ts <u>C</u>H), 125.7 (C**5**), 124.8 (C**9**), 118.6 (C**6**), 83.2 (Boc <u>C</u>(CH$_3$)$_3$), 52.8 (C**1**), 32.3 (C**3**), 27.7 (C**2**), 27.7 (Boc (<u>C</u>H$_3$)$_3$) 26.0 (TBS (<u>C</u>H$_3$)$_3$), 21.8 (Ts C<u>H</u>$_3$), 18.4 (TBS <u>C</u>(CH$_3$)$_3$), 10.1 (C**10**), 8.2 (C**11**,C**12**), -4.1 (TBS Si(<u>C</u>H$_3$)$_2$). HRMS (ESI^+) Calculated for $C_{30}H_{45}NNaO_6SSi$: 598.2629. Found $[M+Na]^+$: 598.2615.

***tert*-Butyl (3-(3-cyclopropyl-4-hydroxyphenyl)propyl)(tosyloxy)carbamate (5d)**

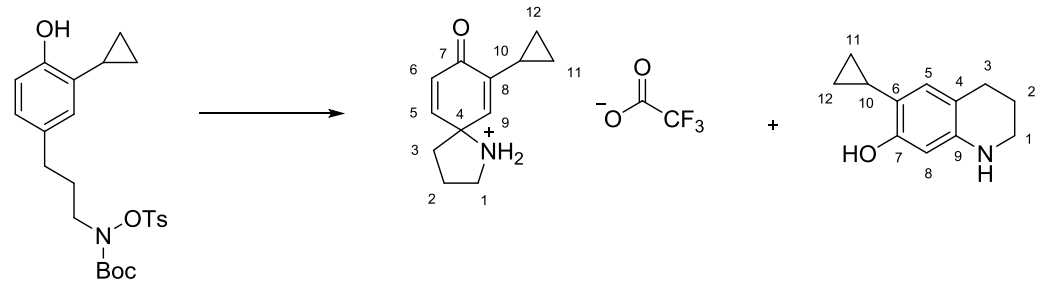


5d

General procedure D: *tert*-Butyl (3-(4-((*tert*-butyldimethylsilyl)oxy)-3-cyclopropylphenyl)propyl) (tosyloxy)carbamate (0.58 g, 1.00 mmol) and 1:1 TBAF/AcOH solution (0.1 M in THF, 1.00 mmol) in THF (20 mL) were employed. Purification by flash column chromatography (20 % EtOAc/hexane) afforded **5d** (0.37 g, 81 % yield) as a colorless solid; m.p.: 82 - 83 ^oC (EtOAc/hexane); R_f = 0.2 (20 % EtOAc/hexane); ν_{max} / cm^{-1} (solid) 3472 (m, br), 2988 (m), 2930 (m), 1693 (s); ^1H NMR (400 MHz, $CDCl_3$) δ 7.84 (2H, d, *J* = 8.1 Hz, Ts ArC<u>H</u>), 7.33 (2H, d, *J* = 8.0 Hz, Ts ArC<u>H</u>), 6.90 (1H, dd, *J* = 8.2, 2.1 Hz, C**5**-<u>H</u>), 6.86 (1H,

d, *J* = 2.2 Hz, C**9**-H), 6.76 (1H, d, *J* =8.1 Hz, C**6**-H), 5.35 (1H, s, OH), 3.61 (2H, app. br s, C**1**-H_2), 2.48 (2H, t, *J* = 7.8 Hz, C**3**-H_2), 2.45 (3H, s, Ts CH_3), 1.95 - 1.84 (2H, m, C**2**-H_2), 1.83 - 1.76 (1H, m, C**10**-H), 1.21 (9H, s, Boc (CH_3)$_3$), 0.98 - 0.93 (2H, m, C**11**/C**12**-H_2), 0.66 - 0.63 (2H, m, C**11**/C**12**-H_2); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.6 (C=O), 153.7 (C**7**), 145.8 (Ts ArC), 132.9 (C**4**), 131.4 (Ts, ArC), 129.8 (2 × Ts, ArCH), 129.6 (2 × Ts, ArCH), 128.5 (C**9**), 127.5 (C**5**), 127.5 (C**8**), 114.6 (C**6**), 83.3 (Boc C(CH$_3$)$_3$), 52.8 (C**1**), 32.2 (C**3**), 27.8 (C**2**), 27.7 (Boc (CH$_3$)$_3$), 21.8 (Ts CH$_3$), 9.5 (C**10**), 5.6 (C**11**,C**12**). HRMS (ESI$^+$) Calculated for $C_{24}H_{31}NNaO_6S$: 484.1764. Found [M+Na]$^+$: 484.1750.

7-Cyclopropyl-1-azaspiro[4.5]deca-6,9-dien-8-one trifluoroacetate (7d) ***and*** **6-cyclopropyl-1,2,3,4-tetrahydroquinolin-7-ol (8d)**



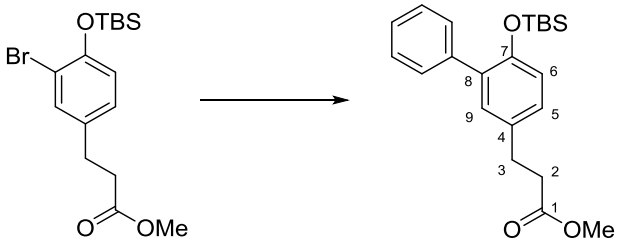
5d **7d** **8d**

General procedure E: *tert*-Butyl (3-(3-cyclopropyl-4-hydroxyphenyl)propyl)(tosyloxy) carbamate (**5d**) (92.3 mg, 0.20 mmol) and TFA (31.0 μL, 0.40 mmol) in TFE (2 mL) were employed. After stirring at r.t. for 24 h, purification by flash column chromatography (EtOAc) afforded the title compounds **7d** (32.1 mg, 53 %) and **8d** (12.8 mg, 34 %) as yellow solids.

Data for **7d**: m.p.: 99 - 101 ºC (EtOAc/hexane); R_f = 0.1 (EtOAc); ν_{max} / cm^{-1} (solid) 2962 (m), 1667 (s), 1643 (s); ^{1}H NMR (400 MHz, CD_3OD) δ 7.07 (1H, dd, *J* = 10.0, 3.1 Hz, C**5**-H), 6.49 (1H, d, *J* = 3.0 Hz, C**9**-H), 6.43 (1H, dd, *J* = 10.1, 1.3 Hz, C**6**-H), 3.66 - 3.56 (2H, m, C**1**-H_2), 2.38 - 2.31 (2H, m, C**2**-H_2), 2.23 - 2.19 (2H, m, C**3**-H_2), 1.94 - 1.88 (1H, m, C**10**-H), 0.91 - 0.87 (2H, m, C**11**/C**12**-H_2), 0.65 - 0.62 (2H, m, C**11**/C**12**-H_2). *The signals corresponding to the NH_2 were not observed.* ^{13}C NMR (101 MHz, CD_3OD) δ 185.4 (C**7**), 144.5 (C**8**), 143.9 (C**5**), 134.6 (C**9**), 131.7 (C**6**), 64.9 (C**4**), 46.3 (C**1**), 37.8 (C**3**), 24.8 (C**2**), 10.0 (C**10**), 8.0 (C**11**/C**12**), 7.9 (C**11**/C**12**). *The signals corresponding to the trifluoroacetate group could not be resolved due to their weak intensity*. HRMS (ESI$^+$) Calculated for $C_{12}H_{16}NO$: 190.1226. Found [M]$^+$ 190.1230.

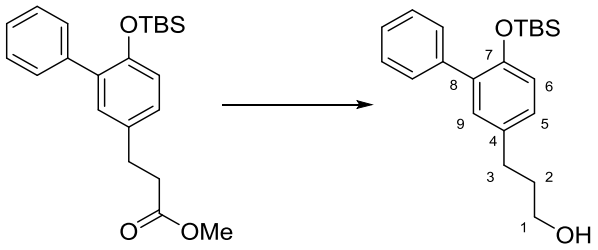
Data for **8d**: m.p.: 108 - 110 °C (EtOAc/hexane); R_f = 0.4 (EtOAc); ν_{max} / cm^{-1} (solid) 3306 (m), 2932 (m), 1614 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.68 (1H, s, C**5**-H), 6.04 (1H, s, C**8**-H), 5.10 (1H, br s, OH), 3.27 - 3.22 (2H, m, C**1**-H_2), 2.66 (2H, t, *J* = 6.4 Hz, C**3**-H_2), 1.93 - 1.87 (2H, m, C**2**-H_2), 1.69 - 1.62 (1H, m, C**10**-H), 0.89 - 0.84 (2H, m, C**11**/C**12**-H_2), 0.57 - 0.53 (2H, m, C**11**/C**12**-H_2); ^{13}C NMR (101 MHz, $CDCl_3$) 154.4 (C**7**), 144.5 (C**9**), 130.1 (C**5**), 116.3 (C**6**), 113.4 (C**4**), 100.1 (C**6**), 42.1 (C**1**), 26.4 (C**3**), 22.7 (C**2**), 8.7 (C**10**), 5.2 (C**11**,C**12**); HRMS (ESI^+) Calculated for $C_{12}H_{16}NO$: 190.1226. Found $[M+H]^+$: 190.1228.

Methyl 3-(6-((*tert*-butyldimethylsilyl)oxy)-[1,1'-biphenyl]-3-yl)propanoate



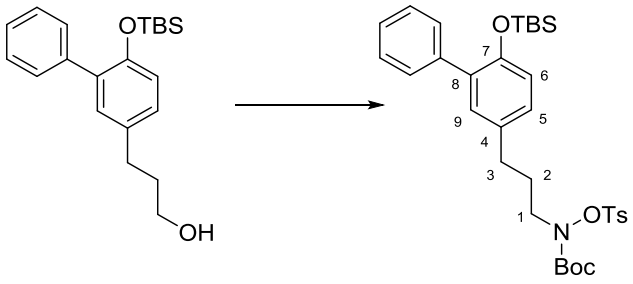
Methyl 3-(3-bromo-4-((*tert*-butyldimethylsilyl)oxy)phenyl)propanoate (1.12 g, 3.00 mmol), phenylboronic acid (1.09 g, 9.00 mmol), K_2CO_3 (1.40 g, 10.2 mmol) and dichloro [1,1'-bis(di-*tert*butylphosphino)ferrocene] palladium(II) ($Pd(dtbpf)Cl_2$) (97.8 mg, 0.15 mmol) in 5:1 PhMe/MeOH (0.12 M) were heated at 110 °C overnight, under an atmosphere of N_2, and monitored by GC-MS. Upon completion, the reaction was cooled to r.t. and filtered through Celite® washing with EtOAc. The crude reaction mixture was then washed with water and the organic layer dried over Na_2SO_4, filtered and concentrated *in vacuo*. Purification by flash column chromatography (5 % EtOAc/hexane) afforded the title compound (0.93 g, 84 %) as a pale yellow oil; R_f = 0.5 (20 % EtOAc/hexane); ν_{max} / cm^{-1} (film) 2952 (m), 2929 (m), 2896 (m), 2857 (m), 1737 (s), 1486 (s), 1253 (s); ^{1}H NMR (440 MHz, $CDCl_3$) δ 7.49 - 7.45 (2H, m, PhCH), 7.39 - 7.33 (2H, m, PhCH), 7.31 - 7.26 (1H, m, PhCH), 7.13 (1H, d, *J* = 2.3 Hz, C**9**-H), 7.03 (1H, dd, *J* = 8.3, 2.4 Hz, C**5**-H_2), 6.82 (1H, d, *J* = 8.2 Hz, C**6**-H_2), 3.67 (3H, s, OCH_3), 2.93 (2H, t, *J* = 7.9 Hz, C**3**-H_2), 2.63 (2H, t, *J* = 7.9 Hz, C**2**-H_2), 0.81 (9H, s, TBS $(CH_3)_3$), -0.07 (6H, s, TBS $Si(CH_3)_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.6 (C**1**), 151.1 (C**7**), 139.2 (C**8**), 133.6 (PhC), 133.5 (C**4**), 130.8 (C**9**), 129.9 (2 × PhCH), 128.1 (C**5**), 127.9 (2 × PhCH), 126.9 (PhCH), 120.5 (C**6**), 51.7 (OCH_3), 36.1 (C**2**), 30.4 (C**3**), 25.7 (TBS $(CH_3)_3$), 18.2 (TBS $SiC(CH_3)_3$), -4.5 (TBS $Si(CH_3)_2$); HRMS (ESI^+) Calculated for $C_{22}H_{30}NaO_{Si}$: 393.1856. Found $[M+Na]^+$: 393.1856.

3-(6-((*tert*-Butyldimethylsilyl)oxy)-[1,1'-biphenyl]-3-yl)propan-1-ol



General procedure B: Methyl 3-(6-((*tert*-butyldimethylsilyl)oxy)-[1,1'-biphenyl]-3-yl)propanoate (0.74 g, 2.00 mmol) and 2.0 eq. $LiAlH_4$ (1 M in THF) in anhydrous Et_2O were employed. Purification by flash column chromatography (20 % EtOAc/hexane) afforded the title compound (0.60 g, 87 %) as a colorless oil; R_f = 0.2 (20 % EtOAc/hexane); ν_{max} / cm^{-1} (film) 3338 (m, br), 2929 (m), 2857 (m), 2884 (m), 1485 (s), 1256 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 - 7.47 (2H, m, PhC<u>H</u>), 7.40 - 7.34 (2H, m, PhC<u>H</u>), 7.32 - 7.26 (1H, m, PhC<u>H</u>), 7.14 (1H, d, *J* = 2.3 Hz, C**9**-<u>H</u>), 7.04 (1H, dd, *J* = 8.2, 2.4 Hz, C**5**-<u>H</u>), 6.84 (1H, d, *J* = 8.2 Hz, C**6**-<u>H</u>), 3.69 (2H, t, *J* = 6.4 Hz, C**1**-<u>H_2</u>), 2.69 (2H, t, *J* = 7.7 Hz, C**3**-<u>H_2</u>), 1.94 - 1.87 (2H, m, C**3**-<u>H_2</u>), 1.38 (1H, br s, O<u>H</u>), 0.82 (9H, s, TBS (C<u>H_3</u>)$_3$), -0.06 (6H, s, TBS Si(C<u>H_3</u>)$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.8 (C**7**), 139.3 (C**8**), 134.9 (C**4**), 133.4 (Ph<u>C</u>), 130.9 (C**9**), 129.9 (2 × Ph<u>C</u>H), 128.2 (C**5**), 127.9 (2 × Ph<u>C</u>H), 126.8 (Ph<u>C</u>H), 120.4 (C**6**), 62.5 (C**1**), 34.5 (C**2**), 31.4 (C**3**), 25.7 (TBS (<u>C</u>H_3)$_3$), 18.2 (TBS Si<u>C</u>(CH_3)$_3$), -4.5 (TBS Si(<u>C</u>H_3)$_2$); HRMS (ESI^+) Calculated for $C_{21}H_{30}NaO_2Si$: 365.1907. Found $[M+Na]^+$: 365.1924.

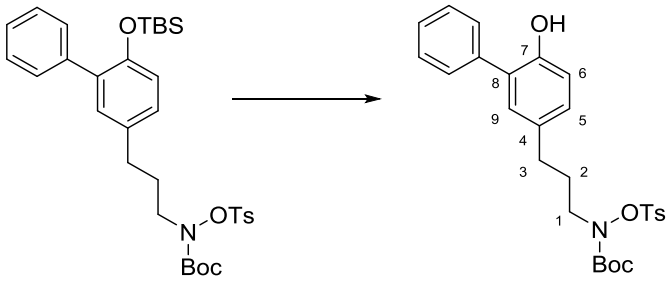
***tert*-Butyl(3-(6-((*tert*-butyldimethylsilyl)oxy)-[1,1'-biphenyl]-3-yl)propyl)(tosyloxy) carbamate**



General procedure C: 3-(6-((*tert*-Butyldimethylsilyl)oxy)-[1,1'-biphenyl]-3-yl)propan-1-ol (**54a**) (0.48 g, 1.40 mmol), PPh_3 (0.44 g, 1.68 mmol), DIAD (0.33 ml, 1.68 mmol) and TsONHBoc (0.48 g, 1.68 mmol) in anhydrous THF (6 mL) were employed. Purification by flash column chromatography (5 % EtOAc/hexane) afforded the title compound (0.74 g, 87%)

as a colorless solid; m.p.: 95 - 96 °C (EtOAc/hexane); R_f = 0.5 (EtOAc/hexane); ν_{max} / cm^{-1} (solid) 2985 (m), 2955 (m), 2937 (m), 1715 (s), 1365 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (2H, d, *J* = 8.2 Hz, Ts ArC<u>H</u>), 7.50-7.47 (2H, m, PhC<u>H</u>), 7.40 - 7.26 (5H, m, 3 × PhC<u>H</u>, 2 × Ts ArC<u>H</u>), 7.09 (1H, d, *J* = 2.3 Hz, C**9**-<u>H</u>), 7.01 (1H, dd, *J* = 8.2, 2.3 Hz, C**5**-<u>H</u>), 6.82 (1H, d, *J* = 8.2 Hz, C**6**-<u>H</u>), 3.64 (2H, app. br s, C**1**-<u>H_2</u>), 2.57 (2H, t, *J* = 7.8 Hz, C**3**-<u>H_2</u>), 2.44 (3H, s, Ts C<u>H_3</u>), 2.01 - 1.88 (2H, m, C**2**-<u>H_2</u>), 1.21 (9H, s, Boc (C<u>H_3</u>)$_3$), 0.81 (9H, s, TBS (C<u>H_3</u>)$_3$), -0.08 (6H, s, TBS Si(C<u>H_3</u>)$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.5 (C=O), 150.9 (C**7**), 145.8 (Ts Ar<u>C</u>), 139.3 (Ph<u>C</u>), 134.2 (C**4**), 133.4 (C**8**), 131.4 (Ts Ar<u>C</u>), 130.8 (C**9**), 129.9 (2 × Ph<u>C</u>H), 129.8 (2 × Ts Ar<u>C</u>H), 129.6 (2 × Ts Ar <u>C</u>H), 128.1 (C**5**), 127.9 (2 × Ph<u>C</u>H), 126.8 (Ph<u>C</u>H), 120.4 (C**6**), 83.3 (Boc <u>C</u>(CH$_3$)$_3$), 52.8 (C**1**), 32.2 (C**3**), 27.8 (Boc (<u>C</u>H$_3$)$_3$), 27.7 (C**2**), 25.7 (TBS (<u>C</u>H$_3$)$_3$), 21.8 (Ts <u>C</u>H$_3$), 18.2 (TBS Si<u>C</u>(CH$_3$)$_3$), -4.5 (TBS Si(<u>C</u>H$_3$)$_2$); HRMS (ESI$^+$) Calculated for $C_{33}H_{45}NNaO_6SSi$: 634.2629. Found $[M+Na]^+$: 634.2609.

***tert*-Butyl (3-(6-hydroxy-[1,1'-biphenyl]-3-yl)propyl)(tosyloxy)carbamate (5e)**

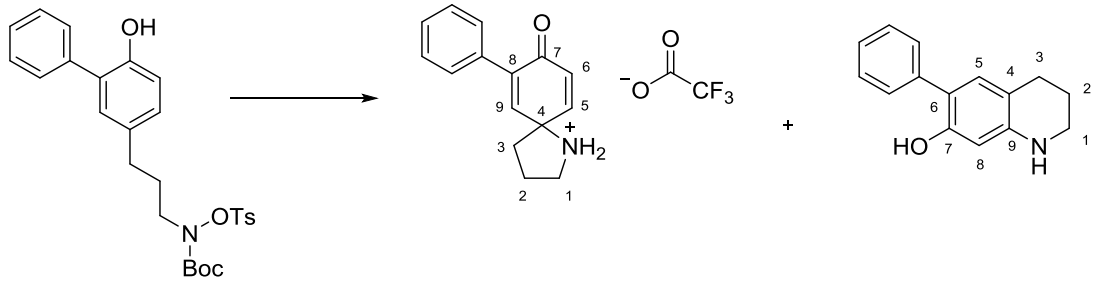


5e

General procedure D: *tert*-Butyl(3-(6-((*tert*-butyldimethylsilyl)oxy)-[1,1'-biphenyl]-3-yl)propyl) (tosyloxy)carbamate (0.61 g, 1.00 mmol) and 1:1 TBAF/AcOH solution (0.1 M in THF, 1.00 mmol) in THF (20 mL) were employed. Purification by flash column chromatography (20 % EtOAc/petroleum ether) afforded **5e** (0.41 g, 82 %) as a colorless solid; m.p.: 108 - 110 °C (EtOAc/hexane); R_f = 0.2 (20 % EtOAc/hexane); ν_{max} / cm^{-1} (film) 3467 (m, br), 2980 (m), 2930 (m), 1719 (s), 1368 (s), 1176 (s), 1151 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (2H, d, *J* = 8.4 Hz, Ts ArC<u>H</u>), 7.51 - 7.46 (4H, m, PhC<u>H</u>), 7.42 - 7.36 (1H, m, PhC<u>H</u>), 7.32 (2H, d, *J* = 8.0 Hz, Ts ArC<u>H</u>), 7.07 - 7.03 (2H, m C**5**, C**9**-<u>H</u>), 6.90 (1H, d, *J* = 8.2 Hz, C**6**-<u>H</u>), 5.17 (1H, s, O<u>H</u>), 3.65 (2H, app. br s, C**1**-<u>H_2</u>), 2.57 (2H, t, *J* = 7.8 Hz, C**3**-<u>H_2</u>), 2.44 (3H, s, Ts C<u>H_3</u>), 2.01 - 1.87 (2H, m, C**2**-<u>H_2</u>), 1.22 (9H, s, Boc (C<u>H_3</u>)$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.6 (C=O), 150.8 (C**7**), 145.8 (Ts Ar<u>C</u>), 137.3 (Ph<u>C</u>), 133.5 (C**4**), 131.4 (Ts Ar<u>C</u>), 130.1 (C**9**), 129.8 (2 × Ph<u>C</u>H), 129.7 (2 × Ts Ar<u>C</u>H), 129.4 (2 × Ts Ar<u>C</u>H), 129.2 (2 × Ph<u>C</u>H), 129.0

(C**5**), 128.1 (C**8**), 127.9 (PhC<u>H</u>), 115.9 (C**6**), 83.4 (Boc <u>C</u>(CH_3)$_3$), 52.7 (C**1**), 32.1 (C**3**), 27.7 (Boc (<u>C</u>H_3)$_3$), 27.7 (C**2**), 21.8 (Ts C<u>H</u>$_3$); HRMS (ESI$^+$) Calculated for $C_{27}H_{31}NNaO_6S$: 520.1764. Found $[M+Na]^+$: 520.1766.

7-Phenyl-1-azaspiro[4.5]deca-6,9-dien-8-one trifluoroacetate (7e) ***and*** **6-Phenyl-1,2,3,4-tetrahydroquinolin-7-ol (8e)**



5e **7e** **8e**

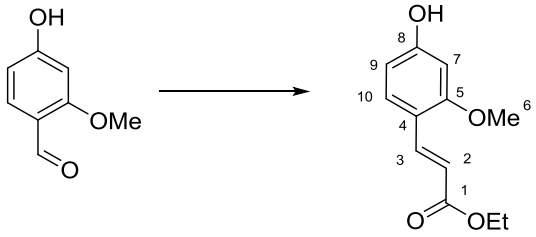
General procedure E: *tert*-Butyl (3-(6-hydroxy-[1,1'-biphenyl]-3-yl)propyl)(tosyloxy) carbamate (**5e**) (74.6 mg, 0.15 mmol) and TFA (23 μL, 0.30 mmol) in anhydrous TFE (1.5 mL) were employed. After stirring at r.t. for 46 h, purification by flash column chromatography (EtOAc) afforded the title compounds **7e** (26.0 mg, 51 %) and **8e** (11.7 mg, 35 %) as yellow solids.

Data for **7e**: m.p.: 136 - 138 ^{o}C (EtOAc/hexane); R_f = 0.1 (5% MeOH/CH_2Cl_2); ν_{max} / cm^{-1} (film) 3374 (m, br), 2975 (m), 1665 (s), 1640 (s); ^{1}H NMR (400 MHz, CD_3OD) δ 7.46 - 7.37 (5H, m, PhC<u>H</u>), 7.14 (1H, dd, *J* = 10.0, 3.3 Hz, C**5**-<u>H</u>), 7.09 (1H, d, *J* = 3.2 Hz, C**9**-<u>H</u>), 6.52 (1H, d, *J* = 10.0 Hz, C**6**-<u>H</u>), 3.70-3.63 (2H, m, C**1**-<u>H</u>$_2$), 2.45-2.30 (4H, m, C**2**-<u>H</u>$_2$, C**3**-<u>H</u>$_2$). *The signals corresponding to the N<u>H</u>$_2$ were not observed.* ^{13}C NMR (101 MHz, CD_3OD) δ 184.4 (C**7**), 143.6 (C**5**), 142.1 (C**8**), 141.0 (C**6**), 135.6 (Ph<u>C</u>), 132.2 (C**6**), 130.0 (2 × Ph<u>C</u>H), 129.9 (Ph<u>C</u>H), 129.2 (2 × Ph<u>C</u>H), 65.2 (C**4**), 46.5 (C**1**), 37.9 (C**3**), 24.9 (C**2**). *The signals corresponding to the trifluoroacetate group could not be resolved due to their weak intensity*. HRMS (ESI$^+$) Calculated for $C_{15}H_{16}NO$: 226.1226. Found $[M]^+$: 226.1229.

Data for **8e**: m.p.: 91 - 94 ^{o}C (EtOAc/hexane); R_f = 0.4 (5% MeOH/CH_2Cl_2); ν_{max} / cm^{-1} (solid) 3405 (br m), 2925 (m), 2852 (m), 1622 (s), 1488 (s), 1160 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 - 7.40 (4H, m, PhC<u>H</u>), 7.33 - 7.28 (1H, m, PhC<u>H</u>), 6.84 (1H, s, C**5**-<u>H</u>), 6.11 (1H, s, C**8**-<u>H</u>), 4.98 (1H, br s), 4.04 (1H, br s), 3.32 - 3.29 (2H, m, C**1**-<u>H</u>$_2$), 2.73 (2H, t, *J* = 6.4 Hz, C**3**-<u>H</u>$_2$), 1.97 - 1.91 (2H, m, C**2**-<u>H</u>$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.3 (C**7**), 145.4 (C**9**), 137.7

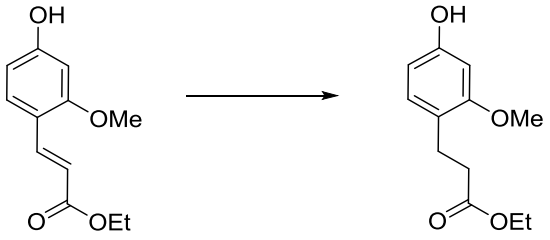
(Ph<u>C</u>), 130.8 (C**5**), 129.1 (2 × Ph<u>C</u>H), 128.9 (2 × Ph<u>C</u>H), 126.8 (Ph<u>C</u>H), 117.3 (C**6**), 114.2 (C**4**), 100.5 (C**8**), 41.9 (C**1**), 26.2 (C**3**), 22.4 (C**2**); HRMS (ESI^+) Calculated for $C_{15}H_{16}NO$: 226.1226. Found $[M+H]^+$: 226.1232.

Ethyl (*E*)-3-(4-hydroxy-2-methoxyphenyl)acrylate



General procedure F: 4-Hydroxy-2-methoxybenzaldehyde (3.04 g, 20.0 mmol) and ethyl 2-(triphenyl-phosphaneylidene) acetate (10.5 g, 30.0 mmol) in CH_2Cl_2 (20 mL) were employed. Purification by flash column chromatography (20 % EtOAc/pentane) afforded the title compound (3.54 g, 80 %) as a colorless solid; m.p.: 144 - 146 ^oC (EtOAc/hexane); R_f = 0.2 (20 % EtOAc/hexane); ν_{max} / cm^{-1} (solid) 3322 (br m), 1675 (s); ^1H NMR (400 MHz, $(CD_3)_2CO$) δ 7.88 (1H, d, *J* = 16.0 Hz, C**3**-<u>H</u>), 7.50 (1H, d, *J* = 8.4 Hz, C**10**-<u>H</u>), 6.53 (1H, d, *J* = 2.3 Hz, C**7**-<u>H</u>), 6.49 (1H, dd, *J* = 8.4, 2.3 Hz, C**9**-<u>H</u>), 6.39 (1H, d, *J* = 16.0 Hz, C**2**-<u>H</u>) 4.18 (2H, q, *J* = 7.1 Hz, OC<u>H</u>$_2$), 3.88 (3H, s, C**6**), 1.27 (3H, t, *J* = 7.1 Hz, $CH_2C\underline{H}_3$); ^{13}C NMR (101 MHz, $(CD_3)_2CO$) δ 168.0 (C**1**), 162.1 (C**8**), 161.0 (C**6**), 140.5 (C**3**), 131.2 (C**10**), 115.8 (C**4**), 115.8 (C**2**), 108.9 (C**9**), 100.0 (C**7**), 60.4 (O<u>C</u>H$_3$), 56.0 (C**6**), 14.8 ($CH_2\underline{C}H_3$); HRMS (ESI^+) Calculated for $C_{12}H_{14}NaO_4$: 245.0784. Found $[M+Na]^+$: 245.0784.

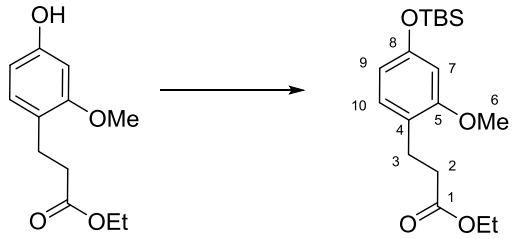
Ethyl 3-(4-hydroxy-2-methoxyphenyl)propanoate[9]



General procedure G: Ethyl (*E*)-3-(4-hydroxy-2-methoxyphenyl)acrylate (2.22 g, 10.0 mmol) and 10 wt.% Pd/C (5 mol%) in EtOH (30 mL) were employed. Purification by Flash column chromatography (20% EtOAc/hexane) afforded the title compound (1.80 g, 80%) as a colorless solid; R_f = 0.2 (20 % EtOAc/hexane); ^1H NMR (400 MHz, $CDCl_3$) δ 6.94 (2H, d, *J* =

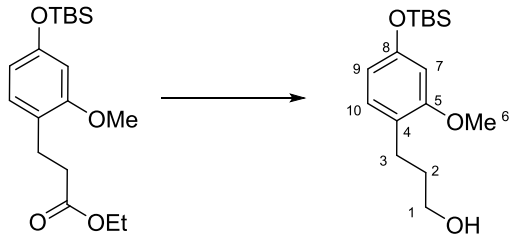
8.0 Hz), 6.38 (1H, d, *J* = 2.4 Hz), 6.31 (1H, dd, *J* = 8.0, 2.4 Hz), 4.13 (2H, q, *J* = 7.2 Hz), 3.74 (3H, s), 2.85 (2H, t, *J* = 8.0 Hz), 2.57 (2H, t, *J* = 8.0 Hz), 1.24 (3H, t, *J* = 7.2 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.3, 158.6, 155.8, 130.4, 120.7, 106.7, 99.0, 60.6, 55.3, 34.8, 25.6, 14.30. *Spectroscopic properties were consistent with the data available in the literature*.[9]

Ethyl 3-(4-((*tert*-butyldimethylsilyl)oxy)-2-methoxyphenyl)propanoate



Ethyl 3-(4-hydroxy-2-methoxyphenyl)propanoate (1.68 g, 7.50 mmol), *tert*-butyldimethylsilyl chloride (1.36 g, 9.00 mmol), and imidazole (1.28 g, 18.75 mmol) in DMF (15 mL) were employed. Purification by flash column chromatography (20 % EtOAc/pentane) afforded the title compound (1.31 g, 52 %) as a colorless oil; R_f = 0.4 (20 % EtOAc/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.95 (1H, d, *J* = 8.7 Hz, C**10**-H), 6.36 - 6.32 (2H, m, C**7**-H, C**9**-H), 4.11 (2H, q, *J* = 7.1 Hz, OCH_2), 3.77 (3H, s, C**6**-H_3), 2.85 (2H, t, *J* = 7.8 Hz, C**3**-H_2), 2.55 (2H, t, *J* = 7.8 Hz, C**2**-H_2), 1.23 (3H, t, *J* = 7.1 Hz, CH_2CH_3), 0.98 (9H, s, TBS (CH_3)$_3$), 0.20 (6H, s, TBS Si(CH_3)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.6 (C**1**), 158.3 (C**5**), 155.4 (C**8**), 130.1 (C**10**), 121.8 (C**4**), 111.3 (C**9**), 103.4 (C**7**), 60.3 (OCH_2), 55.3 (C**6**), 34.7 (C**2**), 25.9 (TBS (CH_3)$_3$), 25.7 (C**3**), 18.3 (TBS SiC(CH_3)$_3$), 14.4 (CH_2CH_3), -4.3 (TBS Si(CH_3)$_2$); HRMS (ESI$^+$) Calculated for $C_{18}H_{30}NaO_4Si$: 361.1806. Found [M+Na]$^+$: 361.1821.

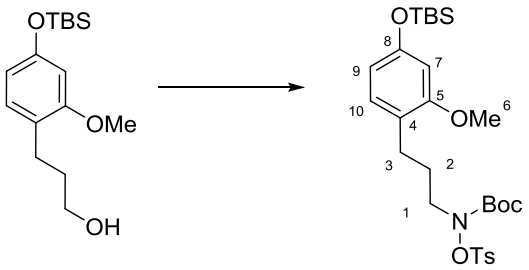
3-(4-((*tert*-Butyldimethylsilyl)oxy)-2-methoxyphenyl)propan-1-ol



General procedure B: Ethyl 3-(4-((*tert*-butyldimethylsilyl)oxy)-2-methoxyphenyl)propanoate (1.01 g, 3.00 mmol) and 1.5 eq. $LiAlH_4$ (1M in THF) in anhydrous Et_2O (15 mL) were employed. Purification by flash column chromatography (33 %

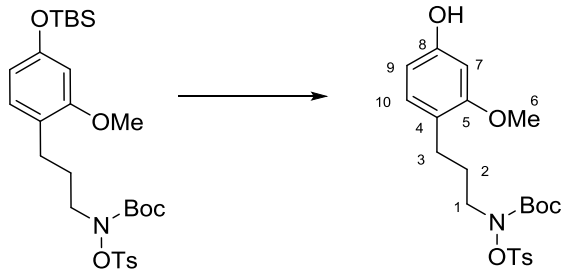
EtOAc/hexane) afforded the title compound (0.65 mg, 73 %) as a colorless oil; R_f = 0.3 (33 % EtOAc/hexane); ν_{max} / cm^{-1} (film) 3351 (br m), 2952 (m), 2930 (m), 2857 (m), 1607 (m), 1503 (s); ^1H NMR (400 MHz, $CDCl_3$) δ 6.95 (1H, d, *J* = 8.4 Hz, C**10**-H), 6.40 - 6.36 (2H, m, C**7**-H, C**9**-H), 3.79 (3H, s, C**6**-H_3), 3.58 (2H, t, *J* = 6.2 Hz, C**1**-H_2), 2.64 (2H, t, *J* = 7.3 Hz, C**3**-H_2), 1.84 - 1.74 (3H, m, C**2**-H_2, OH), 0.99 (9H, s, TBS (CH_3)$_3$), 0.20 (6H, s, TBS Si(CH_3)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.2 (C**5**), 155.1 (C**8**), 130.3 (C**10**), 122.8 (C**4**), 111.8 (C**9**), 103.5 (C**7**), 62.1 (C**1**), 55.5 (C**6**), 33.2 (C**2**), 25.8, (TBS (CH_3)$_3$) 25.4 (C**3**), 18.3 (TBS C(CH_3)$_3$) , -4.3 (TBS Si(CH_3)$_2$); HRMS (ESI^+) Calculated for $C_{16}H_{28}NaO_3Si$: 319.1700. Found $[M+Na]^+$: 319.1707.

***tert*-Butyl (3-(4-((*tert*-butyldimethylsilyl)oxy)-2-methoxyphenyl)propyl)(tosyloxy) carbamate**



General procedure C: 3-(4-((*tert*-Butyldimethylsilyl)oxy)-2-methoxyphenyl)propan-1-ol (0.53 g, 1.80 mmol), PPh_3 (0.56 g, 2.16 mmol), DIAD (0.42 mL, 2.16 mmol) and TsONHBoc (0.62 g, 2.16 mmol) in anhydrous THF (10 mL) were employed. Purification by flash column chromatography afforded the title compound (0.94 g, 92 %) as a colorless oil; R_f = 0.5 (33 % EtOAc/hexane); ν_{max} / cm^{-1} (film) 2955 (m), 2930 (m), 1721 (s), 1504 (s), 1158 (s); ^1H NMR (400 MHz, $CDCl_3$) δ 7.84 (2H, d, *J* = 8.3 Hz, Ts ArCH), 7.32 (2H, d, *J* = 8.3 Hz, Ts ArCH), 6.90 (1H, d, *J* = 8.0 Hz, C**10**-H), 6.36 - 6.33 (2H, m, C**7**, C**9**-H), 3.75 (3H, s, C**6**-H_3), 3.69 - 3.48 (2H, m, C**1**-H_2), 2.49 (2H, t, *J* = 8.0 Hz, C**3**-H_2), 2.44 (3H, s, Ts CH_3), 1.94 - 1.78 (2H, m, C**2**-H_2), 1.22 (9H, s, Boc (CH_3)$_3$), 0.99 (9H, s, TBS (CH_3)$_3$), 0.20 (6H, s, TBS Si(CH_3)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.2 (C**5**), 155.6 (C=O), 155.2 (C**8**), 145.7 (Ts ArC), 131.5 (Ts ArC), 129.8 (2 × Ts ArCH), 129.6 (2 × Ts ArCH), 122.4 (C**4**), 11.4 (C**9**), 103.5 (C**7**), 83.2 (Boc C(CH_3)$_3$), 55.3 (C**6**), 53.1 (C**1**), 27.8 (Boc (CH_3)$_3$), 26.7 (C**3**), 26.1 (C**2**), 25.9 (TBS (CH_3)$_3$), 21.8 (Ts CH_3), 18.4 (TBS SiC(CH_3)$_3$), -4.2 (TBS Si(CH_3)$_2$); HRMS (ESI^+) Calculated for $C_{28}H_{43}NNaO_7SSi$: 588.2422. Found $[M+Na]^+$: 588.2419.

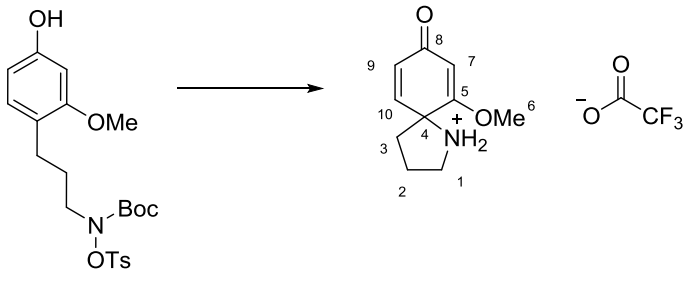
***tert*-Butyl (3-(4-hydroxy-2-methoxyphenyl)propyl)(tosyloxy)carbamate (5f)**



5f

General procedure D: *tert*-Butyl (3-(4-((*tert*-butyldimethylsilyl)oxy)-2-methoxyphenyl) propyl)(tosyloxy)carbamate (0.56 g, 1.00 mmol) and 1:1 TBAF/AcOH solution (0.1 M in THF, 1.00 mmol) in THF (20 mL) were employed. Purification by flash column chromatography (33 % EtOAc/hexane) afforded **5f** (0.38 g, 84 %) as a colorless viscous oil; R_f = 0.25 (33 % EtOAc/hexane); ν_{max} / cm^{-1} (film) 3422 (br m), 2936 (m), 1720 (m), 1368 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (2H, d, *J* = 8.3 Hz, Ts ArCH), 7.32 (2H, d, *J* = 8.3 Hz, Ts ArCH), 6.90 (1H, d, *J* = 8.0 Hz, C**10**-H), 6.38 (1H, d, *J* = 2.4 Hz, C**7**-H), 6.32 (1H, dd, *J* =8.0, 2.4 Hz, C**9**-H_2), 4.67 (1H, br s, OH), 3.76 (3H, s, C**6**-H_3), 3.70 - 3.48 (2H, m, C**1**-H_2), 2.48 (2H, t, *J* = 7.7 Hz, C**3**-H_2), 2.43 (3H, s, Ts CH_3), 1.94 - 1.78 (2H, m, C**2**-H_2), 1.22 (9H, s, Boc $(CH_3)_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.5 (C**5**), 155.7 (C=O), 155.3 (C**8**), 145.7 (Ts ArC), 131.4 (Ts ArC), 130.1 (C**10**), 129.8 (2 × Ts ArCH), 129.6 (2 × Ts ArCH), 121.7 (C**4**), 106.6 (C**9**), 98.9 (C**7**), 83.3 (Boc C$(CH_3)_3$), 55.4 (C**6**), 53.1 (C**1**), 27.8 (Boc $(CH_3)_3$), 26.7 (C**3**), 26.1 (C**2**), 21.8 (Ts CH_3); HRMS (ESI^+) Calculated for $C_{22}H_{29}NNaO_7S$: 474.1557. Found $[M+Na]^+$: 474.1566.

6-Methoxy-1-azaspiro[4.5]deca-6,9-dien-8-one trifluoroacetate (7f)

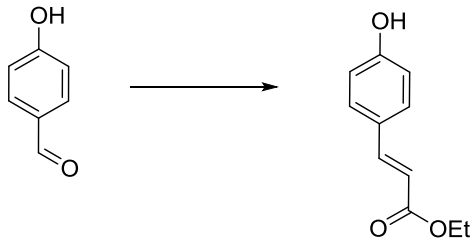


5f **7f**

General procedure E: ***t*ert**-Butyl (3-(4-hydroxy-2-methoxyphenyl)propyl)(tosyloxy) carbamate (**5f**) (67.7 mg, 0.15 mmol) and TFA (23 μL) in TFE (1.5 mL) were stirred at r.t. for 39 h until completion by TLC analysis. Purification by flash column chromatography (EtOAc)

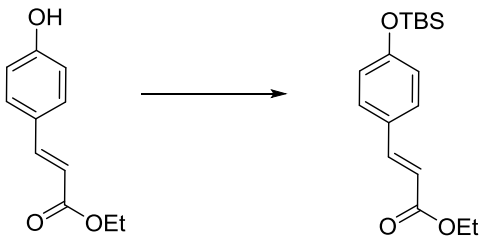
afforded **7f** (32.6 mg, 74 %) as a viscous yellow oil; R_f = 0.1 (5 % MeOH/CH_2Cl_2); ν_{max} / cm^{-1} (film) 2987 (m), 2901 (m), 1665 (s), 1636 (m), 1602 (s); ^{1}H NMR (400 MHz, CD_3OD) δ 6.93 (1H, d, *J* = 10.0 Hz, C**10**-H), 6.29 (1H, dd, *J* = 10.0, 1.6 Hz, C**9**-H) 5.79 (1H, d, *J* = 1.6 Hz, C**7**-H), 3.89 (3H, s, C**6**-H_3), 3.66 - 3.54 (2H, m, C**1**-H_2), 2.53 - 2.46 (1H, m, C**3**-H), 2.40 - 2.22 (3H, m, C**3**-H', C**2**-H_2). *The signals corresponding to the NH_2 were not observed.* ^{13}C NMR (400 MHz, CD_3OD) δ 187.4 (C**8**), 171.2 (C**5**), 141.4 (C**10**), 130.0 (C**9**), 104.2 (C**7**), 65.6 (C**4**), 57.6 (C**6**), 48.7 (C**1**), 38.0 (C**3**), 26.0 (C**2**). *The signals corresponding to the trifluoroacetate group could not be resolved due to their weak intensity*. HRMS (ESI^+) Calculated for $C_{10}H_{14}NO_2$: 180.1019. Found $[M+H]^+$: 180.1021.

Ethyl (*E*)-3-(4-hydroxyphenyl)acrylate[10]



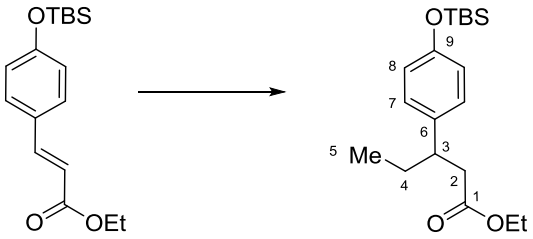
General procedure F: 4-Hydroxybenzaldehyde (4.88 g, 40.0 mmol) and ethyl (triphenylphosphoranylidene)acetate (20.9 g, 60.0 mmol) in CH_2Cl_2 (40 mL) were employed. Purification by flash column chromatography (20 % EtOAc/hexane) afforded the title compound (6.56 g, 85 %) as a colorless solid; R_f = 0.5 (33 % EtOAc/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (1H, d, *J* = 16.0 Hz), 7.42 (2H, d, *J* = 8.6 Hz), 6.86 (2H, d, *J* = 8.3 Hz), 6.30 (1H, d, *J* = 16.0 Hz), 6.14 (1H, br s), 4.27 (2H, q, *J* = 7.1 Hz), 1.34 (3H, t, *J* = 7.1 Hz); ^{13}C NMR (101 MHz) δ 168.1, 158.1, 144.9, 132.4, 130.1, 127.2, 116.1, 115.5, 115.1, 60.8, 14.5. *Spectroscopic properties were consistent with the data available in the literature*.[10]

Ethyl (*E*)-3-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)acrylate[11]



To a solution of Ethyl (*E*)-3-(4-hydroxyphenyl)acrylate (3.84 g, 20.0 mmol) in DMF (20 mL) were added *tert*-butyldimethylsilyl chloride (3.60 g, 24.0 mmol) and imidazole (3.40 g, 50.0 mmol) and the reaction was stirred overnight at r.t. until completion by TLC analysis. Purification by flash column chromatography (20 % EtOAc/ hexane) afforded the title compound (5.13 g, 84 %) as a colorless oil; R_f = 0.4 (10 % EtOAc/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (1H, d, *J* = 16.0 Hz), 7.41 (2H, d, *J* = 8.6 Hz), 6.83 (2H, d, *J* =8.5 Hz), 6.30 (1H, d, *J* = 16.0 Hz), 4.25 (2H, q, *J* = 7.3 Hz), 1.33 (3H, t, *J* = 7.3 Hz), 0.98 (9H, s, TBS ($C\underline{H}_3)_3$), 0.22 (6H, s, TBS Si($C\underline{H}_3)_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.5, 157.9, 144.4, 129.8, 127.9, 120.6, 116.1, 60.4, 25.8, 18.4, 14.5, -4.2. *Spectroscopic properties were consistent with the data available in the literature.* [11]

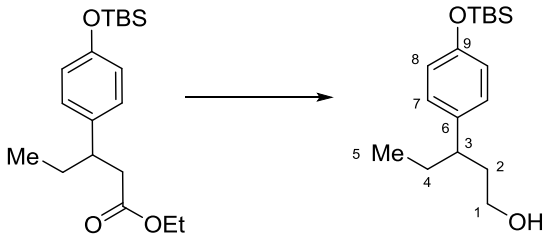
Ethyl 3-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)pentanoate



CuI (2.86 g, 15.0 mmol) in anhydrous Et_2O (60 mL) was stirred under nitrogen at room temperature until a suspension was observed. The mixture was cooled to -20 °C and EtMgBr (3.0 M solution in Et_2O, 37.5 mmol) was added. After stirring for 5 min, a solution of ethyl (*E*)-3-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)acrylate (4.6 g, 15.0 mmol) in anhydrous Et_2O (15 mL) was added dropwise over 1 h. After stirring at -20 °C for 4 h, MeOH (15 mL) and sat. aq. NH_4Cl (60 mL) were sequentially added and the mixture was warmed to r.t. After extracting with Et_2O (3 × 20 mL), the combined organic extracts were dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. Purification by flash column chromatography (20 % EtOAc/hexane) afforded the title compound (4.36 g, 86 %) as a pale yellow oil; R_f = 0.5 (10 % EtOAc/hexane); ν_{max} / cm^{-1} (film) 2958 (m), 2930 (m), 2858 (m), 1735 (s), 1509 (s), 1252 (s), 1165 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.02 (2H, d, *J* = 8.4 Hz, C**7**-$\underline{H}$), 6.75 (2H, d, *J* = 8.6 Hz, C**8**-$\underline{H}$), 4.02 (2H, q, *J* = 7.1 Hz, $OC\underline{H}_2CH_3$), 2.97 - 2.89 (1H, m, C**3**-$\underline{H}$), 2.59 (1H, dd, *J* = 14.9, 7.0 Hz, C**2**-$\underline{H}$), 2.50 (1H, dd, *J* = 14.8, 8.3 Hz, C**2**-$\underline{H}$'), 1.73 - 1.61 (1H, m, C**4**-$\underline{H}$), 1.59 - 1.49 (1H, m, C**4**-$\underline{H}$'), 1.12 (3H, t, *J* = 7.1 Hz, $OCH_2C\underline{H}_3$), 0.97 (9H, s, TBS ($C\underline{H}_3)_3$), 0.77 (3H, t *J* = 7.3 Hz, C**5**-$\underline{H}_3$), 0.18 (6H, s, TBS Si($C\underline{H}_3)_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.7 (C**1**),

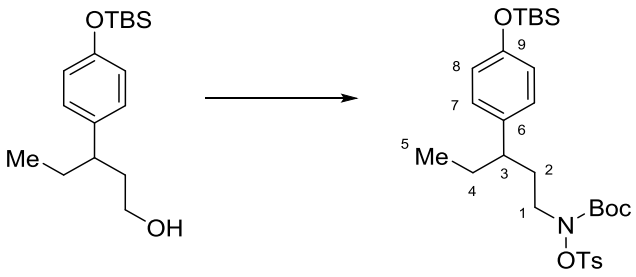
154.1 (C**9**), 136.6 (C**6**), 128.5 (C**7**), 119.9 (C**8**), 60.2 (O<u>C</u>H$_2$CH$_3$), 43.4 (C**3**), 41.9 (C**2**) 29.4 (C**4**), 25.8 (TBS (<u>C</u>H$_3$)$_3$), 18.3 (TBS Si<u>C</u>(CH$_3$)$_3$), 14.3 (OCH$_2$<u>C</u>H$_3$), 12.0 (C**5**), -4.4 (TBS Si(<u>C</u>H$_3$)$_2$); HRMS (ESI$^+$) Calculated for $C_{19}H_{32}NaO_3Si$: 359.2013. Found [M+Na]$^+$: 359.2016.

3-(4-((*tert*-Butyldimethylsilyl)oxy)phenyl)pentan-1-ol



General procedure B: Ethyl 3-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)pentanoate (4.10 g, 12.2 mmol), 1.0 eq. $LiAlH_4$ (1M in THF) and anhydrous Et_2O were employed. The title compound (3.03 g, 84 %) was obtained as a colorless oil which was used without further purification; R_f = 0.3 (20 % EtOAc/hexane); ν_{max} / cm^{-1} (film) 3354 (br m), 2956 (m), 2929 (m), 2858 (m), 1607 (m), 1508 (s), 1253 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.00 (2H, d, *J* = 8.4 Hz, C**7**-<u>H</u>), 6.76 (2H, d, *J* = 8.5 Hz, C**8**-<u>H</u>), 3.55 - 3.43 (2H, m, C**1**-<u>H</u>$_2$), 2.55 - 2.47 (1H, m, C**3**-<u>H</u>), 1.94 - 1.87 (1H, m, C**2**-<u>H</u>), 1.79 - 1.72 (1H, m, C**2**-<u>H</u>'), 1.70 - 1.61 (1H, m, C**4**-<u>H</u>), 1.57 - 1.49 (1H, m, C**4**-<u>H</u>'), 0.98 (9H, s, TBS (C<u>H</u>$_3$)$_3$), 0.77 (3H, t, *J* = 7.4 Hz, C**5**-<u>H</u>$_3$), 0.19 (6H, s, TBS Si(C<u>H</u>$_3$)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.0 (C**9**), 137.6 (C**6**), 128.6 (C**7**-H), 120.0 (C**8**-H), 61.5 (C**1**), 43.7 (C**3**), 39.6 (C**2**), 30.1 (C**4**), 25.8 (TBS C(<u>C</u>H$_3$)$_3$), 18.3 (TBS <u>C</u>(CH$_3$)$_3$), 12.2 (C**5**), -4.3 (TBS Si(<u>C</u>H$_3$)$_2$); HRMS (ESI$^+$) Calculated for $C_{17}H_{30}NaO_2Si$: 317.1907. Found [M+Na]$^+$: 317.1917.

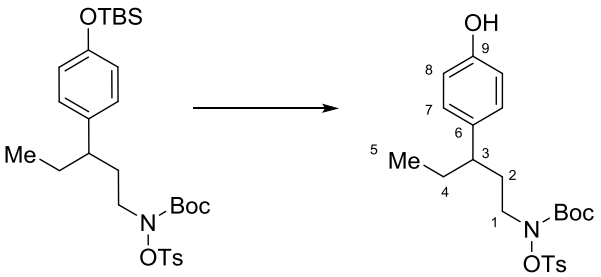
***tert*-Butyl (3-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)pentyl)(tosyloxy)carbamate**



General procedure C: 3-(4-((*tert*-Butyldimethylsilyl)oxy)phenyl)pentan-1-ol (2.94 g, 10.0 mmol), PPh_3 (3.15 g, 12.0 mmol mmol), DIAD (2.36 mL, 12.0 mmol) and TsONHBoc (3.44

g, 12.0 mmol) in anhydrous THF (40 mL) were employed. Purification by flash column chromatography (5 % EtOAc/hexane) afforded the title compound (5.35 g, 95 %) as a colorless oil; R_f = 0.6 (20 % EtOAc/hexane); ν_{max} / cm^{-1} (film) 2962 (m), 2931 (m), 1721 (s), 1509 (s), 1382 (s), 1369 (s), 1253 (s), 1191 (s), 1155 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (2H, d, *J* = 8.2 Hz, Ts ArC<u>H</u>), 7.28 (2H, d, *J* = 8.2 Hz, Ts ArC<u>H</u>), 6.93 (2H, d, *J* = 8.4 Hz, C**7**-<u>H</u>), 6.74 (2H, d, *J* = 8.4 Hz, C**8**-<u>H</u>), 3.48 - 3.19 (2H, m, C**1**-<u>H_2</u>), 2.42 (3H, s, Ts C<u>H_3</u>), 2.33 - 2.26 (1H, m, C**3**-<u>H</u>), 1.94 (1H, app. br s, C**2**-<u>H</u>), 1.76 (1H, app. br s, C**2**-<u>H</u>'), 1.66 - 1.57 (1H, m, C**4**-<u>H</u>), 1.53 - 1.43 (1H, m, C**4**-<u>H</u>'), 1.22 (9H, s, Boc (C<u>H_3</u>)$_3$), 0.98 (9H, s, TBS (C<u>H_3</u>)$_3$), 0.73 (3H, t, *J* = 7.3 Hz, C**5**-<u>H_3</u>), 0.18 (6H, s, TBS Si(C<u>H_3</u>)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) 155.5 (Boc C=O), 154.0 (C**9**), 145.7 (Ts Ar<u>C</u>), 136.9 (C**6**), 131.4 (Ts Ar<u>C</u>), 129.7 (2 × Ts ArC<u>H</u>), 129.6 (2 × Ts ArC<u>H</u>), 128.4 (C**7**), 120.0 (C**8**) 83.2 (Boc <u>C</u>(CH$_3$)$_3$), 52.0 (C**1**), 44.6 (C**3**), 32.0 (C**2**), 30.1 (C**4**), 27.8 (Boc (<u>C</u>H$_3$)$_3$), 25.8 (TBS C(<u>C</u>H$_3$)$_3$), 21.8 (Ts <u>C</u>H$_3$), 18.3 (TBS <u>C</u>(CH$_3$)$_3$), 12.1 (C**5**) , -4.3 (TBS (<u>C</u>H$_3$)$_2$); HRMS (ESI$^+$) Calculated for $C_{29}H_{45}NO_6SSi$: 586.2629. Found $[M+Na]^+$: 586.2628.

***tert*-Butyl (3-(4-hydroxyphenyl)pentyl)(tosyloxy)carbamate (5g)**

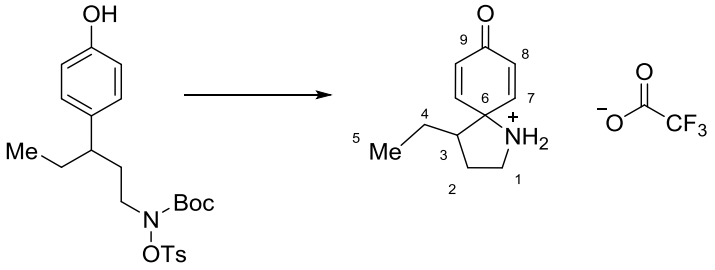


5g

General procedure D: *tert*-Butyl (3-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)pentyl) (tosyloxy)carbamate (2.82 g, 5.0 mmol) and 1:1 TBAF/HOAc (0.1 M in THF, 5.0 mmol) in THF (50 mL) were employed. Purification by flash column chromatography (20 % EtOAc/hexane) afforded **5g** (1.80 g, 80 %) as a colorless solid; m.p.: 93 - 95 ^{o}C (EtOAc/hexane); R_f = 0.4 (33 % EtOAc/hexane); ν_{max} / cm^{-1} (film) 3436 (br m), 2965 (m), 2930 (m), 1720 (s), 1514 (s), 1368 (s), 1191 (s), 1177 (s), 1153 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (2H, d, *J* = 8.0 Hz, Ts ArC<u>H</u>), 7.28 (2H, d, *J* = 8.1 Hz, Ts ArC<u>H</u>), 6.95 (2H, d, *J* = 8.5 Hz C**7**-<u>H</u>), 6.74 (2H, d, *J* 8.5 Hz, C**8**-<u>H</u>), 4.93 (1H, br s, O<u>H</u>), 3.51 - 3.16 (2H, app. br s, C**1**-<u>H_2</u>), 2.42 (3H, s, Ts C<u>H_3</u>), 2.34 - 2.27 (1H, m, C**3**-<u>H</u>), 1.95 (1H, app. br s, C**2**-<u>H</u>), 1.77 (1H, app. br

s, C**2**-H'), 1.66 - 1.54 (1H, m, C**4**-H), 1.52 - 1.43 (1H, m, C**4**-H'), 1.22 (9H, s, Boc (CH_3)$_3$), 0.73 (3H, t, *J* = 7.3 Hz, C**5**-H_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.6 (C=O), 154.1 (C**9**), 145.8 (Ts ArC), 136.3 (C**6**), 131.3 (Ts ArC), 129.7 (2 × Ts ArCH), 129.6 (2 × Ts ArCH), 128.7 (C**7**), 115.4 (C**8**), 83.4 (Boc C(CH$_3$)$_3$), 51.9 (C**1**), 44.5 (C**3**), 32.0 (C**2**), 30.1 (C**4**), 27.8 (Boc (CH$_3$)$_3$), 21.8 (Ts CH$_3$), 12.05 (C**5**); HRMS (ESI$^+$) Calculated for $C_{23}H_{31}NNaO_6S$: 472.1764. Found $[M+H]^+$: 472.1763.

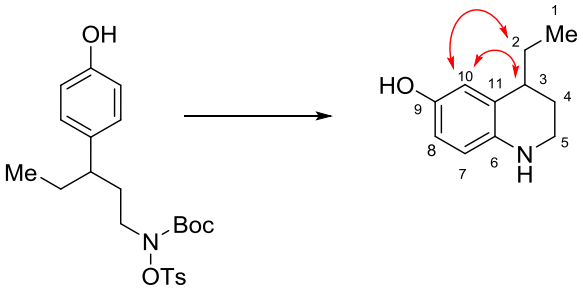
4-Ethyl-1-azaspiro[4.5]deca-6,9-dien-8-one trifluoroacetate (7g)



5g **7g**

General procedure E: *tert*-Butyl (3-(4-hydroxyphenyl)pentyl)(tosyloxy)carbamate (**5g**) (89.9 mg, 0.20 mmol) and TFA (31 μL, 0.40 mmol) in anhydrous TFE (2 mL) were employed. Purification by flash column chromatography (EtOAc) afforded **7g** (40.0 mg, 69 %) as a red/brown oil; R_f = 0.1 (5 % MeOH/CH_2Cl_2); ν_{max} / cm^{-1} 2966 (m), 1673 (s), 1636 (m), 1404 (m), 1201 (s), 1134 (s);); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.93 (1H, dd, *J* = 10.3, 3.2 Hz, C**7**-H), 6.78 (1H, dd, *J* = 10.6, 3.2 Hz, C**7**-H'), 6.43 - 6.36 (2H, m, C**8**-H_2), 3.62 - 3.45 (2H, m, C**1**-H_2), 2.53 - 2.44 (1H, m, C**3**-H), 2.40 - 2.31 (1H, m, C**2**-H), 1.93 - 1.81 (1H, m, C**2**-H'), 1.31 - 1.23 (1H, m, C**4**-H), 1.14 - 1.05 (1H, m, C**4**-H'), 0.91 (3H, *J* = 7.4 Hz, C**5**-H_3); *The signals corresponding to the NH_2 were not observed.* ^{13}C (101 MHz, $CDCl_3$) δ 183.5 (C=O), 143.7 (C**7**), 139.6 (C**7'**), 132.4 (C**8**), 132.0 (C**8'**), 65.5 (C**6**), 50.8 (C**3**), 43.4 (C**1**), 29.3 (C**2**), 21.5 (C**4**), 12.5 (C**5**); *The signals corresponding to the trifluoroacetate group could not be resolved due to their weak intensity*. HRMS (ESI$^+$) Calculated for $C_{11}H_{16}NO^+$: 178.1226. Found $[M+H]^+$: 178.1225.

4-Ethyl-1,2,3,4-tetrahydroquinolin-7-ol (8g)

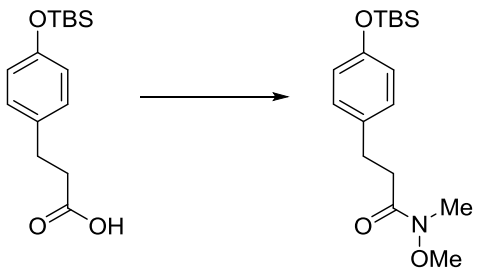


5g **8g**

To a solution of *tert*-Butyl (3-(4-hydroxyphenyl)pentyl)(tosyloxy)carbamate (**5g**) (67.4 mg, 0.15 mmol) in anhydrous TFE (2.3 mL, 0.067 M) at r.t. was added TFA (1.7 µL, 0.022 mmol). The reaction was heated to 60 °C and stirred overnight monitoring by TLC analysis. Purification by flash column chromatography (gradient, eluent 33 % EtOAc/hexane – 100 % EtOAc (*a small amount < 1% Et_3N was added to the eluent*)) afforded **8g** (20.4 mg, 77 %) as a yellow oil; R_f = 0.5 (EtOAc); ν_{max} / cm^{-1} (film) 3145 (m, br), 2971 (m), 1618 (m), 1467 (m), 1238 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.55 (1H, s, C**10**-H), 6.49 (1H, d, *J* = 8.0 Hz, C**8**-H), 6.41 (1H, d, *J* = 8.5 Hz, C**7**-H), 4.20 (2H, br s), 3.28 - 3.16 (2H, m, C**5**-H_2), 2.62 - 2.56 (1H, m, C**3**-H), 1.95 - 1.87 (1H, m, C**4**-H), 1.80 - 1.67 (2H, m, C**4**-H', C**2**-H), 1.56 - 1.45 (1H, m, C**2**-H'), 0.96 (3H, t, *J* = 7.4 Hz, C**1**-H_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.7 (C**9**), 138.1 (C**6**), 127.9 (C**11**), 116.0 (C**7**), 115.9 (C**10**), 114.2 (C**8**), 39.3 (C**5**), 37.2 (C**3**), 29.4 (C**2**), 26.2 (C**4**), 11.7 (C**1**). HRMS (ESI^+) Calculated for $C_{11}H_{16}NO$: 178.1226. Found $[M+H]^+$: 178.1227.

*The regiochemistry of the compound was confirmed by nOe analysis as shown on the compound structure. nOes were observed between C**10**-H and C**3**-H and C**10**-H and C**2**-H_2.*

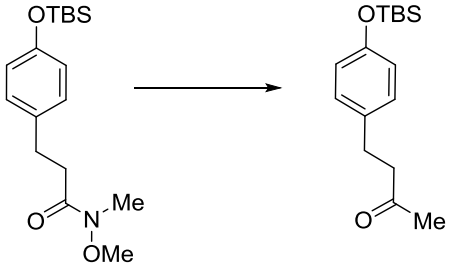
3-(4-((*tert*-Butyldimethylsilyl)oxy)phenyl)-*N*-methoxy-*N*-methylpropanamide[12]



General procedure H: 3-(4-((*tert*-Butyldimethylsilyl)oxy)phenyl)propanoic acid (2.40 g, 8.57 mmol), *N*,*O*-dimethylhydroxylamine hydrochloride (1.17 g, 12.0 mmol), Et_3N (1.67 mL,

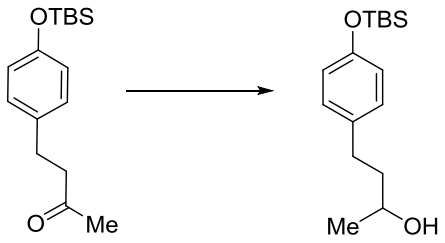
12.0 mmol), 4-dimethylaminopyridine (1.46 g, 12.0 mmol), and *N*,*N*'-dicyclohexylcarbodiimide (2.48 g, 12.0 mmol) were employed. Purification by flash column chromatography (20 % EtOAc/hexane) afforded the title compound (1.97 g, 71 %) as a colorless oil; R_f = 0.2 (33 % EtOAc/hexane); ν_{max} / cm^{-1} 2955 (m), 2930 (m), 2857 (m), 1665 (s), 1509 (s), 1250 (s), 1169 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.06 (2H, d, *J* = 8.0 Hz), 6.75 (2H, d, *J* = 8.0 Hz), 3.57 (3H, s), 3.16 (3H, s), 2.88 (2H, t, *J* = 7.6 Hz), 2.71 - 2.67 (2H, m), 0.97 (9H, s), 0.17 (6H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.7, 153.8, 133.9, 129.2, 119.9, 61.1, 33.9, 32.1, 29.9, 25.6, 18.1, -4.4. *Spectroscopic properties were consistent with the data available in the literature.*[12]

4-(4-((*tert*-Butyldimethylsilyl)oxy)phenyl)butan-2-one[13]



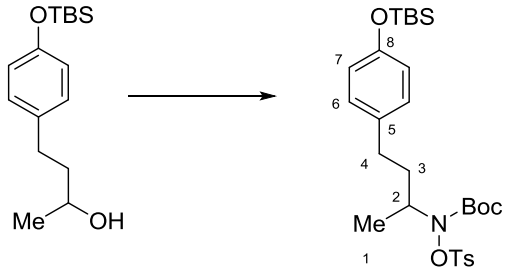
To a solution of 3-(4-((*tert*-Butyldimethylsilyl)oxy)phenyl)-*N*-methoxy-*N*-methylpropanamide (0.69 g, 2.15 mmol) in anhydrous THF (5 mL) at 0 °C was added methylmagnesium bromide (3 M in Et_2O, 1.43 mL, 4.30 mmol) dropwise over 5 min. The reaction mixture was stirred at r.t. for 1.5 h and then a solution of sat. aq. NH_4Cl (5 mL) was added. The aqueous phase was extracted with EtOAc (3 × 5mL) and the combined organic layers were washed with brine (10 mL), dried over Na_2SO_4 and concentrated *in vacuo* to afford the title compound (0.60 g, 99 %) as a colorless oil, which was used without further purification; R_f = 0.6 (33 % EtOAc/hexane); ν_{max} / cm^{-1} 2955 (m), 2929 (m), 2888 (m), 2857 (m), 1716 (s), 1610 (m), 1509 (s), 1361 (m), 1251 (s), 1159 (m), 1168 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.02 (2H, d, *J* = 8.0 Hz), 6.75 (2H, d, *J* = 8.0 Hz), 2.85 - 2.68 (4H, m), 2.12 (3H, s), 0.98 (9H, s), 0.18 (6H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 208.2, 153.9, 133.6, 129.2, 120.1, 45.5, 30.2, 29.1, 25.8, 18.2, -4.3. *Spectroscopic properties were consistent with the data available in the literature.* [13]

4-(4-((*tert*-Butyldimethylsilyl)oxy)phenyl)butan-2-ol[14]



To a solution of 4-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)butan-2-one (0.56 g, 2.14 mmol) in MeOH (10 mL) was slowly added $NaBH_4$ (0.16 g, 4.28 mmol) at 0 ^{o}C. After stirring for 45 min at this temperature the reaction was quenched by addition of water (10 mL) and extracted with Et_2O (3 × 10 mL). The combined organic extracts were washed with brine (10 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo* to afford the title compound (0.55 g, 92 %) as a colorless oil which was used without further purification; R_f = 0.5 (33 % EtOAc/hexane); ν_{max} / cm^{-1} (film) 3339 (m, br), 2957 (m), 2929 (m), 2857 (m), 1609 (m), 1508 (s), 1250 (s), 1168 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.05 (2H, d, *J* = 8.4 Hz), 6.76 (2H, d, *J* = 8.4 Hz), 3.86 - 3.77 (1H, m), 2.72 - 2.57 (2H, m), 1.80 - 1.69 (2H, m), 1.65 - 1.54 (1H, br s), 1.22 (3H, d, *J* = 6.2 Hz), 0.99 (9H, s), 0.19 (6H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.6, 134.7, 129.2, 119.9, 67.5, 41.0, 31.3, 25.7, 23.6, 18.2, -4.4. *Spectroscopic properties were consistent with the data available in the literature*.[14]

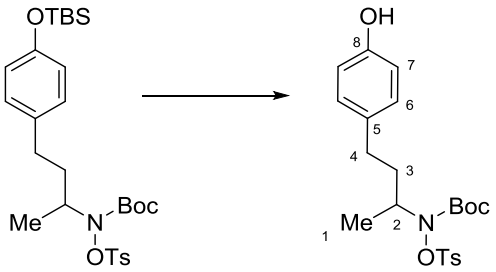
***tert*-Butyl (4-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)butan-2-yl)(tosyloxy)carbamate**



General procedure C: 4-(4-((*tert*-Butyldimethylsilyl)oxy)phenyl)butan-2-ol (0.22 g, 0.77 mmol), PPh_3 (0.24 g, 0.92 mmol), DIAD (0.18 mL, 0.92 mmol) and TsONHBoc (0.26 g, 0.92 mmol) in anhydrous THF (3 mL) were employed. Purification by flash column chromatography (10 % EtOAc/hexane) afforded the title compound (0.34 g, 75 %) as a colorless oil; R_f = 0.6 (20 % EtOAc/hexane); ν_{max} / cm^{-1} (film) 2954 (m), 2930 (m), 2857 (m), 1721 (m), 1509 (s), 1368 (m), 1251 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (2H, d, *J* = 8.4 Hz, Ts ArC<u>H</u>), 7.32 (2H, d, *J* = 8.4 Hz, Ts ArC<u>H</u>), 7.01 (2H, d, *J* = 8.4 Hz, C**6**-<u>H</u>), 6.73 (2H, d, *J* =

8.4 Hz, C**7**-H), 3.97 (1H, app. sextet, *J* = 6.8 Hz, C**2**-H), 2.61 - 2.57 (2H, m, C**4**-H_2), 2.43 (3H, s, Ts CH_3), 2.06 - 1.97 (1H, m, C**3**-H_2), 1.74 - 1.66 (1H, m, C**3**-H'), 1.27 (9H, s, Boc (CH_3)$_3$), 1.21 (3H, d, *J* = 6.8 Hz, C**1**-H_3), 0.97 (9H, s, TBS (CH_3)$_3$), 0.17 (6H, s, TBS Si(CH_3)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.4 (C=O), 153.8 (C**8**), 145.6 (Ts ArC), 134.4 (C**5**), 131.9 (Ts ArC), 129.7 (2 × Ts ArCH), 129.6 (2 × Ts ArCH), 129.3 (C**6**), 119.9 (C**7**), 83.4 (Boc C(CH$_3$)$_3$, 60.8 (C**2**), 32.2 (C**3**), 29.8 (C**4**), 27.8 (Boc (CH$_3$)$_3$, 25.8 (TBS (CH$_3$)$_3$), 21.8 (Ts CH$_3$), 18.3 (TBS SiC(CH$_3$)$_3$), 17.4 (C**1**), -4.4 (TBS Si(CH$_3$)$_2$); HRMS (ESI$^+$) Calculated for $C_{28}H_{43}NNaO_6SSi$: 572.2473. Found [M+Na]$^+$: 572.2465.

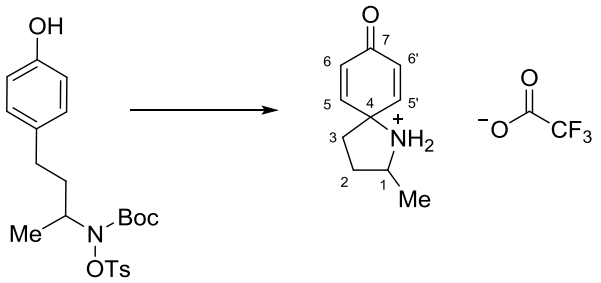
***tert*-Butyl (4-(4-hydroxyphenyl)butan-2-yl)(tosyloxy)carbamate (5h)**



5h

General procedure D: *tert*-Butyl (4-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)butan-2-yl)(tosyloxy) carbamate (0.32 g, 0.58 mmol) and 1:1 TBAF/HOAc solution (0.1 M in THF, 0.58 mmol) in THF (20 mL) were employed. Purification by flash column chromatography (20 % EtOAc/hexane) afforded **5h** (0.19 g, 75 %) as a colorless oil; R_f = 0.2 (20% EtOAc/hexane); ν_{max} / cm^{-1} (film) 3477 (br m), 2979 (m), 1721 (s), 1515 (s), 1369 (s), 1191 (s), 1177 (s), 1156 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (2H, d, *J* = 8.5 Hz, Ts ArCH), 7.31 (2H, d, *J* = 8.5 Hz, Ts ArCH), 7.01 (2H, d, *J* = 7.8 Hz, C**6**-H), 6.74 (2H, d, *J* = 8.3 Hz, C**7**-H), 5.14 (1H, br s, OH), 3.97 (1H, app. sextet, *J* = 7.2 Hz, C**2**-H), 2.58 (2H, t, *J* = 7.5 Hz, C**4**-H_2), 2.42 (3H, s, Ts CH_3), 2.05 - 1.95 (1H, m, C**3**-H), 1.73-1.60 (1H, m, C**3**-H'), 1.27 (9H, s, Boc (CH_3)$_3$), 1.20 (3H, d, *J* = 6.8 Hz, C**1**-H_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.5 (C=O) 153.9 (C**8**), 145.7 (Ts ArC), 133.7 (C**5**), 131.8 (Ts ArC), 129.7 (2 × Ts ArCH), 129.6 (2 × Ts ArCH), 129.5 (C**6**), 115.3 (C**7**), 83.6 (Boc C(CH$_3$)$_3$), 60.8 (C**2**), 36.0 (C**3**) 32.1 (C**4**), 27.8 (Boc C(CH$_3$)$_3$), 21.8 (Ts CH$_3$), 17.4 (C**1**); HRMS (ESI$^+$) Calculated for $C_{22}H_{29}NNaO_6S$: 458.1608. Found [M+Na]$^+$: 458.1597.

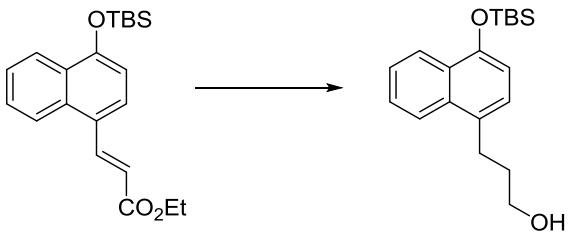
2-Methyl-1-azaspiro[4.5]deca-6,9-dien-8-one trifluoroacetate (7h)



5h **7h**

General procedure E: *tert*-Butyl (4-(4-hydroxyphenyl)butan-2-yl)(tosyloxy)carbamate (**5h**) (93.0 mg, 0.21 mmol) and TFA (32 μL, 0.42 mmol) in TFE (2.1 mL) were stirred at r.t. for 24 h. Purification by flash column chromatography (EtOAc) afforded **7h** (34.0 mg, 58 %) as a yellow/brown oil; R_f = 0.1 (5% MeOH/CH_2Cl_2); ν_{max} / cm^{-1} (film, $CDCl_3$) 2922 (m), 1667 (s), 1635 (m), 1393 (m), 1173 (s), 1133 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (2H, br s, N$\underline{H}_2$), 7.04 (1H, dd, *J* = 10.2, 3.2 Hz, C**5**-$\underline{H}$), 6.95 (1H, dd, *J* = 10.3, 3.2 Hz, C**5**-$\underline{H}$'), 6.33 - 6.32 (1H, m, C**6**-$\underline{H}$), 6.31 - 6.29 (1H, m, C**6**-$\underline{H}$'), 4.05 - 3.96 (1H, m, C**1**-$\underline{H}$), 2.47 - 2.39 (1H, m, C**2**-$\underline{H}$), 2.36 - 2.29 (1H, m, C**3**-$\underline{H}$), 2.24 - 2.17 (1H, m, C**3**-$\underline{H}$'), 2.08 - 1.98 (1H, m, C**2**-H'), 1.46 (3H, d, *J* = 6.6 Hz, C$\underline{H}_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 183.6 (C**7**), 143.6 (C**5**), 143.0 (C**5**), 130.5 (C**6**), 130.4 (C**6**), 63.2 (C**4**), 57.2 (C**1**), 37.1 (C**3**), 32.0 (C**2**), 17.5 ($\underline{C}H_3$); HRMS (ESI^+) Calculated for $C_{10}H_{14}NO$: 164.1070. Found $[M+H]^+$: 164.1068.

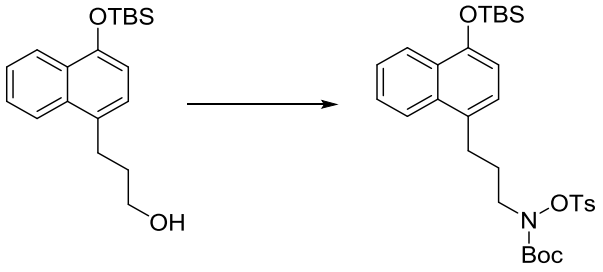
3-(4-((*tert*-Butyldimethylsilyl)oxy)naphthalen-1-yl)propan-1-ol



General procedure B: Ethyl (*E*)-3-(4-((tert-butyldimethylsilyl)oxy)naphthalen-1-yl)acrylate (1.64 g, 4.59 mmol, 1.0 eq.) and 2.0 eq. $LiAlH_4$ (1.0 M in THF) in anhydrous THF (10 mL) were employed. Purification by flash chromatography (gradient, elution 20 - 33 % EtOAc/hexane) afforded the title compound (0.77 g, 53 %) as a colorless oil; R_f = 0.6 (33% EtOAc/hexane); ν_{max} / cm^{-1} (film) 2988 (s), 2901 (s), 1394 (m), 1275 (m), 1260 (m), 1075 (s), 1066 (s), 1057 (s), 750 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 – 8.19 (1H, m), 7.99 (1H, dd, *J*

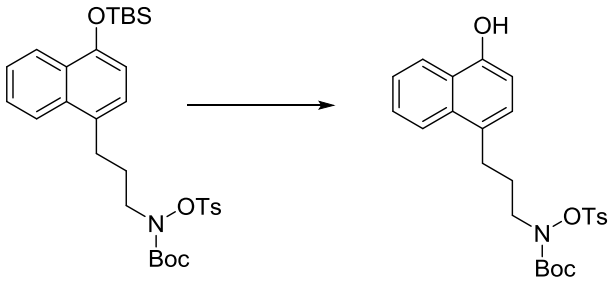
= 8.1, 1.5 Hz), 7.53 – 7.45 (2H, m), 7.18 (1H, d, *J* = 7.7 Hz), 6.79 (1H, d, *J* = 7.7 Hz), 3.74 (2H, t, *J* = 6.4 Hz), 3.10 (2H, dd, *J* = 8.6, 6.7 Hz), 2.08 – 1.90 (2H, m), 1.10 (9H, s), 0.29 (6H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.4, 133.1, 130.6, 128.4, 126.2, 126.0, 124.9, 123.9, 123.5, 112.2, 62.7, 33.8, 28.9, 26.1, 26.0, 18.6, -4.1; HRMS (ESI$^+$) Calculated for $C_{19}H_{28}NaO_2Si$: 339.1751. Found $[M+Na]^+$: 339.1763.

***tert*-Butyl (3-(4-((*tert*-butyldimethylsilyl)oxy)naphthalen-1-yl)propyl)(tosyloxy)carbamate**



To a solution of alcohol (0.75 g, 2.36 mmol), TsONHBoc (0.82 g, 2.84 mmol, 1.2 eq.) and PPh_3 (0.93 g, 2.84 mmol, 1.2 eq.) in anhydrous THF (16 mL) at 0 °C was added a solution of DIAD (0.70 mL, 2.84 mmol, 1.2 eq.) in anhydrous THF (5 mL) dropwise under Argon atmosphere. The reaction mixture was stirred at r.t. overnight before being concentrated *in vacuo* and loaded directly onto silica gel for purification by flash chromatography (gradient, elution 20 % PhMe/hexane - 100% PhMe) to afford the title compound (1.12 g, 81 %) as a colorless solid; m.p.: 87 - 89 ^{o}C (EtOAc/hexane); R_f = 0.7 (33% EtOAc/hexane); ν_{max} / cm^{-1} (solid) 2972 (s), 1722 (m), 1393 (s), 1259 (m), 1156 (m), 1075 (s), 750 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 – 8.15 (1H, m), 7.95 – 7.87 (1H, m), 7.84 (2H, d, *J* = 8.4 Hz), 7.48 (2H, dddd, *J* = 16.6, 8.1, 6.8, 1.5 Hz), 7.30 (2H, d, *J* = 7.8 Hz), 7.13 (1H, d, *J* = 7.7 Hz), 6.77 (1H, d, *J* = 7.7 Hz), 3.70 (2H, s), 2.97 (2H, t, *J* = 7.8 Hz), 2.43 (3H, s), 2.16 – 1.89 (2H, m), 1.19 (9H, s), 1.10 (9H, s), 0.28 (6H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.6, 150.6, 145.8, 133.0, 131.4, 129.8, 129.8, 129.6, 128.4, 126.3, 125.9, 124.9, 123.7, 123.5, 112.1, 83.4, 53.1, 29.7, 27.7, 27.1, 26.1, 21.8, 18.6, -4.1; HRMS (ESI$^+$) Calculated for $C_{31}H_{43}NNaO_6SSi$: 608.2473. Found $[M+Na]^+$: 608.2473.

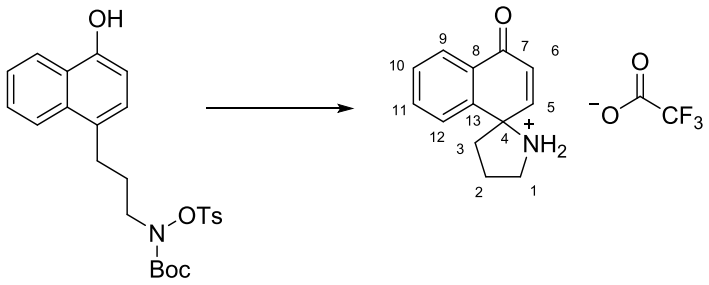
***tert*-Butyl (3-(4-hydroxynaphthalen-1-yl)propyl)(tosyloxy)carbamate (5i)**



5i

General procedure D: *tert*-Butyl (3-(4-((*tert*-butyldimethylsilyl)oxy)naphthalen-1-yl)propyl) (tosyloxy)carbamate (0.97 g, 1.66 mmol) and 1:1 TBAF/AcOH solution (1.0 M in THF, 1,66 mmol) in THF (17 mL) were employed. Purification by flash column chromatography (gradient, eluent 20 - 30% EtOAc/hexane) afforded **5i** (0.53 g, 67%) as a viscous colorless oil; R_f = 0.4 (33% EtOAc/hexane); ν_{max} / cm^{-1} (film) 3417 (br, m), 2980 (m), 2871 (m), 1720 (s), 1589 (m), 1370 (s), 1191 (s), 1178 (s), 1151 (s), 763 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (1H, d, *J* = 7.9 Hz), 7.91 (1H, d, *J* = 8.2 Hz), 7.83 (2H, d, *J* = 8.1 Hz), 7.54 – 7.43 (2H, m), 7.29 (2H, d, *J* = 8.1 Hz), 7.08 (1H, d, *J* = 7.6 Hz), 6.73 (1H, d, *J* = 7.6 Hz), 3.70 (2H, s), 2.95 (2H, t, *J* = 7.9 Hz), 2.42 (3H, s), 2.03 (2H, q, *J* = 12.1, 8.4 Hz), 1.19 (9H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.7, 150.5, 145.8, 132.8, 131.3, 129.8, 129.6, 126.5, 125.8, 125.0, 124.9, 123.7, 122.6, 108.2, 83.5, 53.0, 29.6, 27.7, 27.1, 21.8; HRMS (ESI^+) Calculated for $C_{25}H_{29}NNaO_6S$: 494.1608. Found $[M+Na]^+$: 494.1603.

4*H*-spiro[naphthalene-1,2'-pyrrolidin]-4-one trifluoroacetate (7i)

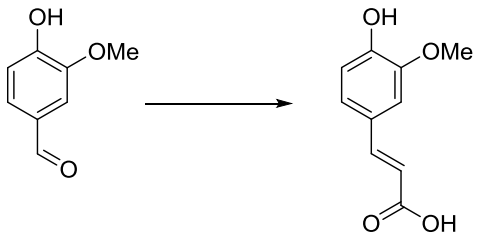


5i **7i**

General procedure E: *tert*-Butyl (3-(4-hydroxynaphthalen-1-yl)propyl)(tosyloxy)carbamate (**5i**) (70.7 mg, 0.150 mmol) and TFA (23 μL, 0.30 mmol) in anhydrous TFE (1.5 mL) were stirred at r.t. for 22 h. Purification by flash column chromatography (EtOAc) afforded **7i** (14.3

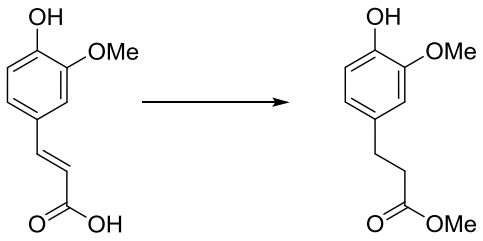
mg, 30 %) as a yellow/brown solid; R_f = 0.1 (5 % MeOH/CH_2Cl_2); ν_{max} / cm^{-1} (solid) 2987 (m), 2971 (m), 1665 (s), 1601 (m); ^{1}H NMR (400 MHz, CD_3OD) δ 8.19 (1H, d, *J* = 7.7 Hz, C**9**-H), 7.88 - 7.82 (2H, m, C**11**-H, C**12**-H), 7.67 (1H, ddd, *J* = 8.1, 6.1, 2.3 Hz, C**10**-H), 7.25 (1H, d, *J* = 10.3 Hz, C**5**-H), 6.61 (1H, d, *J* = 10.3 Hz, C**6**-H), 3.84 - 3.72 (2H, m, C**1**-H_2), 2.71 - 2.62 (1H, m, C**3**-H), 2.57 - 2.48 (3H, m, C**3**-H', C**2**-H_2). *The signals corresponding to the NH_2 were not observed.* ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.0 (C**7**), 144.5 (C**5**), 140.5 (C**13**), 135.4 (C**11**), 132.1 (C**8**), 131.1 (C**10**), 130.7 (C**6**), 128.1 (C**9**), 127.7 (C**12**), 65.9 (C**4**), 47.7 (C**1**), 41.2 (C**3**), 25.8 (C**2**). *The signals corresponding to the trifluoroacetate group could not be resolved due to their weak intensity*. HRMS (ESI$^+$) Calculated for $C_{13}H_{14}NO$: 200.1069. Found $[M+H]^+$: 200.1074.

(*E*)-3-(4-Hydroxy-3-methoxyphenyl)acrylic acid[15]



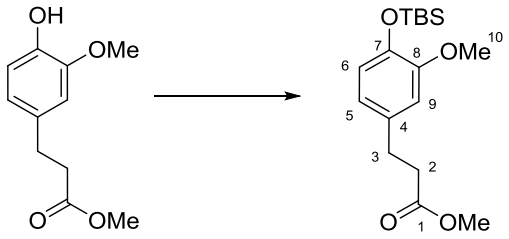
Vanillin (3.04 g, 20.0 mmol) and malonic acid (2.30 g, 22.0 mmol) were added to a solution of aniline (0.22 mL, 2.36 mmol) and pyridine (2.43 mL, 30.0 mmol) in toluene (5 mL). The solution was stirred at refluxing temperature for 2 h. The mixture was cooled to r.t. and neutralised with an aq. 25 % solution of K_2CO_3 (12 mL) followed by careful addition of concentrated HCl (until pH = 3). The resulting precipitate was filtered and washed with ice cold H_2O (10 mL) to afford the title compound (3.0 g, 77 %) as a yellow solid which was used without further purification; R_f = 0.5 (33 % EtOAc); ^{1}H NMR (440 MHz, CD_3OD) δ 7.60 (1H, d, *J* = 15.8 Hz), 7.18 (1H, d, *J* = 2.0 Hz), 7.07 (1H, dd, *J* = 8.2, 2.0 Hz), 6.81 (1H, d, *J* = 8.2 Hz), 6.31 (1H, d, *J* = 15.8 Hz), 3.90 (3H, s); ^{13}C NMR (101 MHz, CD_3OD) δ 171.0, 150.5, 149.4, 146.9, 127.8, 123.9, 116.5, 115.9, 111.7, 56.4. *Spectroscopic properties were consistent with the data available in the literature*.[15]

Methyl 3-(4-hydroxy-3-methoxyphenyl)propanoate[16]



General procedure G: (*E*)-3-(4-Hydroxy-3-methoxyphenyl)acrylic acid (1.94 g, 10.0 mmol) and 10 wt.% Pd/C (5 mol%) in 5:1 EtOAc/MeOH (60 mL) were employed. Purification by flash column chromatography (50 % EtOAc/hexane) afforded the title compound (1.66 g, 80 %) as a yellow oil; R_f = 0.4 (33 % EtOAc/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.83 (1H, d, *J* = 7.9 Hz), 6.72 - 6.66 (2H, m), 5.57 (1H, s), 3.86 (3H, s), 3.67 (3H, s), 2.88 (2H, t, *J* = 7.8 Hz), 2.60 (2H, t, *J* = 7.8 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.5, 146.4, 144.1, 132.5, 120.9, 114.5, 111.0, 55.9, 51.7, 36.2, 30.7. *Spectroscopic properties were consistent with the data available in the literature.*[16]

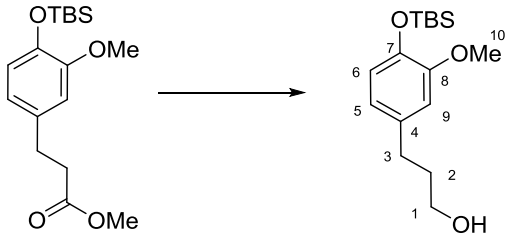
Methyl 3-(4-((*tert*-butyldimethylsilyl)oxy)-3-methoxyphenyl)propanoate



Methyl 3-(4-hydroxy-3-methoxyphenyl)propanoate (1.55 g, 7.40 mmol), *tert*-butydimethylsilyl chloride (1.34 g, 8.90 mmol) and imidazole (0.65 g, 9.60 mmol) in 2.5:1 CH_2Cl_2/DMF (35 mL) were stirred at r.t. overnight and monitored by TLC. Upon completion, the reaction was quenched by addition of H_2O (50 mL), extracted with CH_2Cl_2 (3 × 20 mL), washed with brine (20 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by flash column chromatography (gradient 20 - 33 % EtOAc/hexane) afforded the title compound (1.85 g, 77 %) as a pale yellow oil; R_f = 0.7 (33 % EtOAc/hexane); ν_{max} / cm^{-1} (film) 2952 (m), 2930 (m), 2857 (m), 1738 (s), 1512 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.74 (1H, d, *J* = 8.0 Hz, C**6**-H), 6.67 (1H, d, *J* = 2.0 Hz, C**9**-H), 6.62 (1H, dd, *J* = 8.0 Hz, 2.0 Hz, C**5**-H), 3.77 (3H, s, C**10**-H_3), 3.65 (3H, s, CO_2CH_3), 2.87 (2H, t, *J* = 7.4 Hz, C**3**-H_2), 2.59 (2H, t, *J* = 7.4 Hz, C**2**-H_2), 0.98 (9H, s, TBS (CH_3)$_3$), 0.13 (6H, s, TBS Si(CH_3)$_2$); ^{13}C NMR (101 MHz,

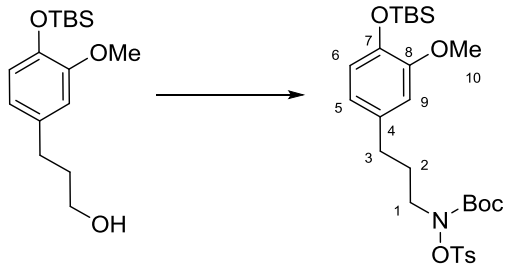
$CDCl_3$) δ 173.5 (C**1**), 150.9 (C**8**), 143.5 (C**7**), 134.1 (C**4**), 120.9 (C**6**), 120.4 (C**5**) 112.5 (C**9**), 55.5 (C**10**), 51.6 ($CO_2\underline{C}H_3$), 36.1 (C**2**), 30.8 (C**3**), 25.8 (TBS ($\underline{C}H_3)_3$), 18.5 (TBS Si$\underline{C}(CH_3)_3$), -4.6 (TBS Si($\underline{C}H_3)_2$). HRMS (ESI^+) Calculated for $C_{17}H_{28}NaO_4Si$: 347.1649. Found $[M+Na]^+$: 347.1661.

3-(4-((*tert*-Butyldimethylsilyl)oxy)-3-methoxyphenyl)propan-1-ol



General procedure B: Methyl 3-(4-((*tert*-butyldimethylsilyl)oxy)-3-methoxyphenyl) propanoate (1.71 g, 5.00 mmol) and 2.0 eq. $LiAlH_4$ (1.0 M in THF) in anhydrous Et_2O (25 mL) were employed to afford the title compound (1.34 g, 90 %) as a pale yellow oil which was used without further purification; R_f = 0.3 (33 % EtOAc/hexane); ν_{max} / cm^{-1} (film) 3357 (m br), 2930 (m), 2885 (m), 2857 (m), 1511 (s); ^1H NMR (400 MHz, $CDCl_3$) δ 6.74 (1H, d, *J* = 8.0 Hz, C**6**-$\underline{H}$), 6.67 (1H, d, *J* = 2.0 Hz, C**9**-$\underline{H}$), 6.62 (1H, dd, *J* = 8.0, 2 Hz, C**5**-$\underline{H}$), 3.78 (3H, s, C**10**-$\underline{H}_3$), 3.65 (2H, t, *J* = 6.4 Hz, C**1**-$\underline{H}_2$), 2.63 (2H, t, *J* = 7.4 Hz, C**3**-$\underline{H}_2$), 1.89 - 1.82 (2H, m, C**2**-$\underline{H}_2$), 0.98 (9H, s, TBS ($C\underline{H}_3)_3$), 0.13 (6H, s, TBS Si($C\underline{H}_3)_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.8 (C**8**), 143.2 (C**7**), 135.3 (C**5**), 120.8 (C**6**), 120.5 (C**5**), 112.6 (C**9**), 62.5 (C**1**), 55.6 (C**10**), 34.4 (C**2**), 31.9 (C**3**), 25.8 (TBS ($\underline{C}H_3)_3$), 18.5 (TBS Si$\underline{C}(CH_3)_3$), -4.6, (TBS Si($\underline{C}H_3)_2$). HRMS (ESI^+) Calculated for $C_{16}H_{28}NaO_3Si$: 319.1700. Found $[M+Na]^+$: 319.1710.

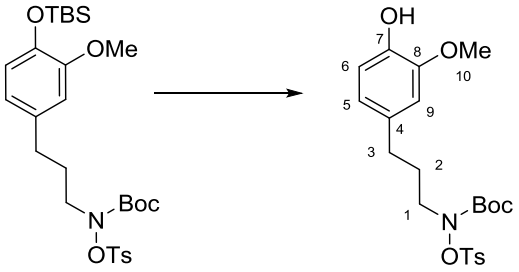
***tert*-Butyl (3-(4-((*tert*-butyldimethylsilyl)oxy)-3-methoxyphenyl)propyl)(tosyloxy) carbamate**



General procedure C: 3-(4-((*tert*-Butyldimethylsilyl)oxy)-3-methoxyphenyl)propan-1-ol (0.59 g, 2.00 mmol), PPh_3 (0.63 g, 2.40 mmol), DIAD (0.47 mL, 2.40 mmol) and TsONHBoc

(0.69 g, 2.40 mmol) in anhydrous THF (10 mL) were employed. Purification by flash column chromatography (10 % EtOAc/hexane) afforded the title compound (0.94 g, 83 %) as a colorless oil; R_f = 0.5 (20 % EtOAc/hexane); ν_{max} / cm^{-1} (film) 2954 (m), 2930 (m), 2857 (m), 1720 (m), 1512 (s); ^{1}H NMR (400 MHz, $CDCl_3$) 7.84 (2H, d, *J* = 8.3 Hz, Ts ArC<u>H</u>), 7.32 (2H, d, *J* = 8.3 Hz, Ts ArC<u>H</u>), 6.74 (1H, d, *J* = 8.0 Hz, C**6**-<u>H</u>), 6.66 (1H, d, *J* = 2.0 Hz, C**9**-<u>H</u>), 6.59 (1H, dd, *J* = 8.0, 2.0 Hz, C**5**-<u>H</u>), 3.79 (3H, s, C**10**-<u>H</u>$_3$), 3.62 (2H, app. br s, C**1**-<u>H</u>$_2$), 2.52 (2H, t, *J* = 7.8 Hz, C**3**-<u>H</u>$_2$), 2.45 (3H, s, Ts C<u>H</u>$_3$), 1.98 - 1.87 (2H, m, C**2**-<u>H</u>$_2$), 1.22 (9H, s, Boc (C<u>H</u>$_3$)$_3$), 0.99 (9H, s, TBS (C<u>H</u>$_3$)$_3$), 0.14 (6H, s, TBS Si(C<u>H</u>$_3$)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.6 (C=O), 150.9 (C**8**), 145.8 (Ts Ar<u>C</u>), 143.3 (C**7**), 134.7 (C**4**), 131.4 (Ts Ar<u>C</u>), 129.8 (2 × Ts Ar<u>C</u>H), 129.7 (2 × Ts Ar<u>C</u>H), 120.8 (C**6**), 120.5 (C**5**), 122.5 (C**9**) 83.3 (Boc <u>C</u>(CH$_3$)$_3$), 55.6 (C**10**), 52.8 (C**1**), 32.6 (C**3**), 27.8 (Boc (<u>C</u>H$_3$)$_3$), 27.6 (C**2**), 25.9 (TBS (<u>C</u>H$_3$)$_3$), 21.8 (Ts <u>C</u>H$_3$), 18.6 (TBS Si<u>C</u>(CH$_3$)$_3$), -4.5 (TBS Si(<u>C</u>H$_3$)$_2$). HRMS (ESI$^+$) Calculated for $C_{28}H_{43}NNaO_7SSi$: 588.2422. Found $[M+Na]^+$: 588.2432.

***tert*-Butyl (3-(4-hydroxy-3-methoxyphenyl)propyl)(tosyloxy)carbamate (5j)**

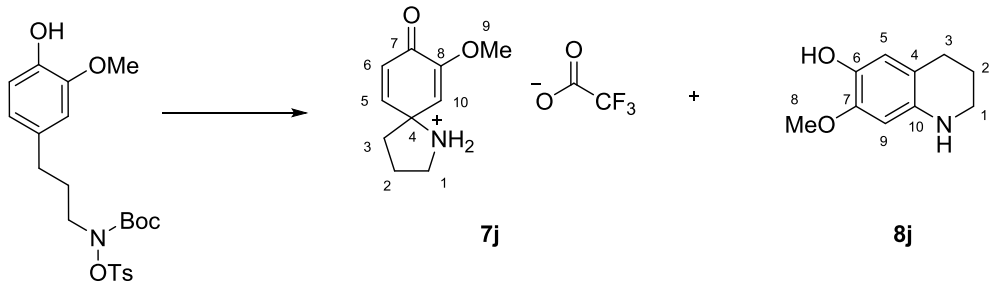


5j

General procedure D: *tert*-Butyl (3-(4-((*tert*-butyldimethylsilyl)oxy)-3-methoxyphenyl) propyl)(tosyloxy)carbamate (0.57 g, 1.0 mmol), and 1:1 TBAF/AcOH solution (0.1 M in THF, 1.0 mmol) in THF (20 mL) were employed. Purification by flash column chromatography (20 % EtOAc/hexane) afforded **5j** (0.28 g, 62 %) as a colorless solid; m.p.: 82 - 84 ^{o}C (EtOAc/hexane); R_f = 0.4 (33 % EtOAc/hexane); ν_{max} / cm^{-1} (solid) 3505 (m, br), 2989 (m), 2964 (m), 2935 (m), 1749 (s), 1514 (m), 1153 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (2H, d, *J* = 8.2 Hz, Ts ArC<u>H</u>), 7.33 (2H, d, *J* = 8.1 Hz, Ts ArC<u>H</u>), 6.82 (1H, d, *J* = 8.0 Hz, C**6**-<u>H</u>), 6.69 (1H, d, *J* = 1.9 Hz, C**9**-<u>H</u>), 6.64 (1H, dd, *J* = 8.0, 1.9 Hz, C**5**-<u>H</u>), 5.47 (1H, s, O<u>H</u>), 3.89 (3H, s, C**10**-<u>H</u>$_3$), 3.60 (2H, app. br s, C**1**-<u>H</u>$_2$), 2.53 (2H, t, *J* = 7.6 Hz, C**3**-<u>H</u>$_2$), 2.45 (3H, s, Ts C<u>H</u>$_3$), 1.97 - 1.87 (2H, m, C**2**-<u>H</u>$_2$), 1.22 (9H, s, Boc (C<u>H</u>$_3$)$_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.6 (C=O), 146.5 (C**8**) 145.8, (Ts Ar<u>C</u>), 143.9 (C**7**), 133.1 (C**4**), 131.3 (Ts Ar<u>C</u>), 129.8 (2 × Ts

ArCH), 129.6 (2 × Ts ArCH), 120.9 (C**5**), 114.3 (C**6**), 110.9 (C**9**), 83.3 (Boc C(CH$_3$)$_3$), 56.1 (C**10**), 52.6 (C**1**), 32.6 (C**3**), 27.7 (Boc (CH$_3$)$_3$), 27.7 (C**2**) 21.8 (Ts CH$_3$). HRMS (ESI$^+$) Calculated for $C_{22}H_{29}NNaO_7S$: 474.1557. Found [M+Na]$^+$: 474.1551.

7-Methoxy-1-azaspiro[4.5]deca-6,9-dien-8-one trifluoroacetate (7j) ***and*** **7-methoxy-1,2,3,4-tetrahydroquinolin-6-ol (8j)**



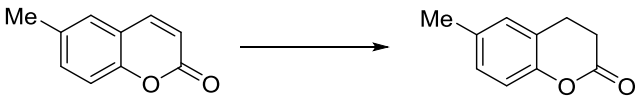
5j **7j** **8j**

General procedure E: *tert*-Butyl (3-(4-hydroxy-3-methoxyphenyl)propyl)(tosyloxy) carbamate (**5j**) (67.7 mg, 0.15 mmol) and TFA (23 μL) in TFE (1.5 mL) were stirred at r.t. for 40 h. Upon completion, the reaction mixture was concentrated *in vacuo*. *An in situ yield was obtained by ^{1}H NMR analysis against 1,3,5-trimethoxybenzene as an internal standard; a 27 % yield of* ***7j*** *and 62 % yield of* ***8j*** *were observed.* Purification by flash column chromatography (EtOAc) afforded **8j** (14.9 mg, 55 %) as a yellow solid, however, **7j** could not be isolated cleanly.

Data for **7j**: *from NMR analysis of crude material:* ^{1}H NMR (400 MHz, CD$_3$OD) δ 7.11 (1H, dd, *J* = 10.0, 2.9 Hz, C**5**-H), 6.46 (1H, d, *J* = 10.0 Hz, C**6**-H), 6.03 (1H, d, *J* = 2.9 Hz, C**10**-H), 3.75 (3H, s, C**9**-H$_2$), 3.68 - 3.60 (2H, m, C**1**-H$_2$), 2.46-2.43 (2H, m, C**2**-H$_2$), 2.33 - 2.27 (2H, m, C**3**-H$_2$); ^{13}C NMR (101 MHz, CD$_3$OD) δ 180.8 (C**7**), 153.5 (C**8**), 144.8 (C**5**), 131.3 (C**6**), 111.5 (C**10**), 66.6 (C**4**), 56.0 (C**9**) 46.1 (C**1**) 38.2 (C**3**), 24.7 (C**2**);

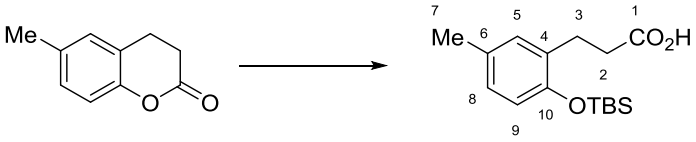
Data for **8j**: m.p.: 76 - 78 ^{o}C (EtOAc/hexane); R_f = 0.7 (EtOAc); ν_{max} / cm^{-1} (solid) 3383 (br m), 3324 (br m), 2926 (m), 1508 (s), 1464 (m), 1443 (m); ^{1}H NMR (400 MHz, CDCl$_3$) δ 6.50 (1H, s, C**5**-H), 6.14 (1H, s, C**9**-H), 3.79 (3H, s, C**8**-H$_3$), 3.25 - 3.20 (2H, m, C**1**-H$_2$), 2.68 (2H, t, *J* = 6.5 Hz, C**3**-H$_2$), 1.94-1.88 (2H, m, C**2**-H$_2$); ^{13}C NMR (101 MHz, CDCl$_3$) δ 144.7 (C**6**), 139.3 (C**10**), 139.1 (C**7**), 113.1 (C**5**), 112.7 (C**4**), 101.7 (C**9**), 57.0 (C**8**), 42.3 (C**1**), 26.7 (C**3**), 22.8 (C**2**); HRMS (ESI$^+$) Calculated for $C_{10}H_{14}NO_2$: 180.1019. Found [M+H]$^+$:180.1027.

6-Methylchroman-2-one[17]



General procedure G: 6-Methylcoumarin (4.80 g, 30.0 mmol) and 5 mol% Pd/C (10 wt. %, 1.50 mmol), in EtOAc (30 mL) were employed. Purification by flash column chromatography afforded the title compound (3.40 g, 70 %) as a colorless solid; R_f = 0.4 (20 % EtOAc/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04 (1H, dd, *J* = 8.1, 1.9 Hz), 6.99 (1H, s), 6.93 (1H, d, *J* = 8.2 Hz), 2.98 - 2.93 (2H, m), 2.79 - 2.73 (2H, m), 2.31 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.9, 149.9, 134.0, 128.8, 128.5, 122.4, 116.7, 29.4, 23.8, 20.8. *Spectroscopic properties were consistent with the data available in the literature*.[17]

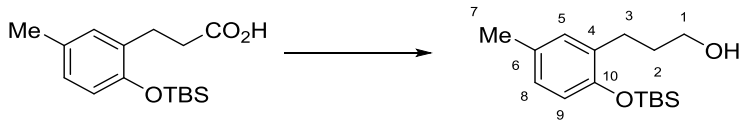
3-(2-((*tert*-Butyldimethylsilyl)oxy)-5-methylphenyl)propanoic acid



To a solution of 6-methylchroman-2-one (1.74 g, 10.0 mmol) in THF (50 mL) was added an aq. 1 M solution of LiOH (33.0 mmol, 58 mL). After stirring at r.t. overnight the pH was acidified to approx. 3 with aq. 1 M HCl. The product was extracted with EtOAc (2 × 20 mL), dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was dissolved in DMF (20 mL) and cooled to 0 °C before *tert*-butyldimethylsilyl chloride (3.32 g, 22.0 mmol) and imidazole (2.24 g, 33.0 mmol) were added. After being stirred at r.t. overnight the reaction was quenched by addition of H_2O (50 mL) and the product was extracted with hexane (3 × 20 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. To the crude product in MeOH (10 mL) and THF (10 mL) was added aq. K_2CO_3 (20.0 mmol, 2.76 g in 30 mL H_2O). After stirring at r.t. overnight the reaction was cooled to 0 °C and quenched with aq. 1 M HCl (30 mL). The mixture was extracted with Et_2O (3 × 20 mL), dried over Na_2SO_4, filtered and concentrated *in vacuo*. Purification by flash column chromatography (20 % EtOAc/hexane) afforded the title compound (1.60 g, 54 %) as a colorless solid; m.p.: 49 - 51 °C (EtOAc/hexane); R_f = 0.4 (20 % EtOAc/hexane); ν_{max} / cm^{-1} (solid) 2961 (m), 2948 (m), 2927 (m), 2900 (m), 1702 (s), 1499 (m), 1252 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.97 (1H, d, *J* = 2.5 Hz, C**5**-H), 6.89 (1H, dd, *J* = 8.3, 2.3 Hz, C**8**-H), 6.69 (1H, d, *J* = 8.3 Hz, C**9**-H), 2.89 (2H, t, *J* = 7.8 Hz, C**3**-H_2), 2.65 (2H, t, *J* = 7.9 Hz, C**2**-H_2), 2.26 (3H, s, C**7**-H_3), 1.01 (9H, s, TBS (CH_3)$_3$), 0.23 (6H, s, TBS

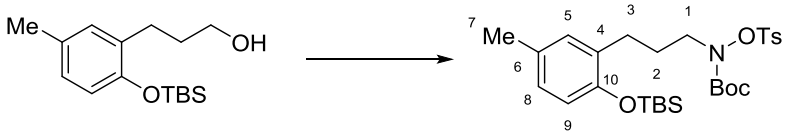
Si(C$\underline{H}_3$)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 179.3 (C**1**), 151.5 (C**10**), 130.9 (C**5**), 130.5 (C**4**), 130.4 (C**6**), 128.0, (C**8**) 118.3 (C**9**), 34.3 (C**2**), 26.2 (C**3**), 25.9 (TBS (C$\underline{H}_3$)$_3$), 20.7 (C**7**), 18.4 (TBS C$\underline{(CH_3)_3}$), -4.0 (TBS Si(C$\underline{H}_3$)$_2$); HRMS (ESI$^+$) Calculated for $C_{16}H_{27}O_3Si$: 295.1724. Found $[M+H]^+$: 295.1739.

3-(2-((*tert*-Butyldimethylsilyl)oxy)-5-methylphenyl)propan-1-ol[18]



General procedure I: 3-(2-((*tert*-Butyldimethylsilyl)oxy)-5-methylphenyl)propanoic acid (1.25 g, 4.26 mmol), Et_3N (0.59 mL, 4.26 mmol), ethylchloroformate (0.41 mL, 4.26 mmol) and $NaBH_4$ (0.40 g, 10.60 mmol) in THF (30 mL) and H_2O (15 mL) were employed. Purification by flash column chromatography (20 % EtOAc/hexane) afforded the title compound (0.83 mg, 60 %) as a colorless oil; R_f = 0.35 (20 % EtOAc/hexane); ν_{max} / cm^{-1} (film) 3334 (m, br), 2953 (m), 2929 (m), 2885 (m), 2858 (m), 1498 (s), 1253 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.94 (1H, d, *J* = 2.3 Hz, C**5**-$\underline{H}$), 6.86 (1H, dd, *J* = 8.2, 2.3 Hz, C**8**-$\underline{H}$), 6.68 (1H, d, *J* = 8.1 Hz, C**9**-$\underline{H}$), 3.61 (2H, t, *J* =6.4 Hz, C**1**-$\underline{H}_2$), 2.65 (2H, t, *J* = 7.4 Hz, C**3**-$\underline{H}_2$), 2.25 (3H, s, C**7**-$\underline{H}_3$), 1.99 - 1.70 (2H, m, C**2**-$\underline{H}_2$), 1.01 (9H, s, TBS (C$\underline{H}_3$)$_3$), 0.22 (6H, s, TBS Si(C$\underline{H}_3$)$_2$); ^{13}C NMR (400 MHz, $CDCl_3$) δ 151.3 (C**10**), 131.9 (C**4**), 131.1 (C**5**), 130.6 (C**6**), 127.4 (C**8**), 118.5 (C**9**), 62.4 (C**1**), 33.3 (C**2**), 26.6 (C**3**), 26.0 (TBS (C$\underline{H}_3$)$_3$), 20.7 (C**7**), 18.4 (TBS C$\underline{(CH_3)_3}$, -4.0 (TBS Si(C$\underline{H}_3$)$_2$). Spectroscopic properties were consistent with the data available in the literature.[18]

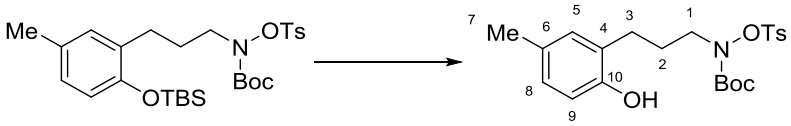
***tert*-Butyl(3-(2-((*tert*-butyldimethylsilyl)oxy)-5-methylphenyl)propyl)(tosyloxy) carbamate**



General procedure C: 3-(2-((*tert*-Butyldimethylsilyl)oxy)-5-methylphenyl)propan-1-ol (0.87 g, 1.58 mmol), PPh_3 (0.50 g, 1.90 mmol), DIAD (0.37 mL, 1.90 mmol) and TsONHBoc (0.54 g, 1.90 mmol) were employed. Purification by flash column chromatography (10 % EtOAc/hexane) afforded the title compound (0.71 mg, 65 %) as a colorless oil; R_f = 0.6 (20 %

EtOAc/hexane); ν_{max} / cm^{-1} (film) 2957 (m), 2929 (m), 2901 (m), 2859 (m), 1721 (m), 1499 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (2H, d, *J* = 8.3 Hz, Ts ArC<u>H</u>), 7.31 (2H, d, *J* = 8.3 Hz, Ts ArC<u>H</u>), 6.92 (1H, d, *J* = 2.3 Hz, C**5**-<u>H</u>), 6.85 (1H, dd, *J* = 8.1, 2.3 Hz, C**8**-<u>H</u>), 6.66 (1H, d, *J* = 8.1 Hz, C**9**-<u>H</u>), 3.62 (2H, app. br s, C**1**-<u>H_2</u>), 2.51 (2H, t, *J* = 7.8 Hz, C**3**-<u>H_2</u>), 2.43 (3H, s, Ts C<u>H_3</u>), 2.25 (3H, s, C**7**-<u>H_3</u>), 1.96 - 1.84 (2H, m, C**2**-<u>H_2</u>), 1.20 (9H, s, Boc (C<u>H_3</u>)$_3$), 1.01 (9H, s, TBS (C<u>H_3</u>)$_3$), 0.21 (6H, s, TBS Si(C<u>H_3</u>)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.5 (C=O), 151.3 (C**10**), 145.6 (Ts Ar<u>C</u>), 131.5 (Ts Ar<u>C</u>), 131.4 (C**4**), 130.8 (C**5**), 130.2 (C**6**), 129.8 (2 × Ts ArC<u>H</u>), 129.6 (2 × Ts Ar<u>C</u>H), 127.5 (C**8**), 118.3 (C**9**), 83.1 (Boc <u>C</u>(CH$_3$)$_3$), 52.9 (C**1**), 27.7 (C**3**), 27.7 (Boc (<u>C</u>H$_3$)$_3$), 26.1 (C**2**), 25.9 (TBS (<u>C</u>H$_3$)$_3$), 21.8 (Ts <u>C</u>H$_3$), 20.6 (C**7**), 18.3 (TBS Si<u>C</u>(CH$_3$)$_3$), -4.1 (TBS Si(<u>C</u>H$_3$)$_2$); HRMS (ESI^+) Calculated for $C_{28}H_{43}NNaO_6SSi$: 572.2473. Found $[M+Na]^+$: 572.2477.

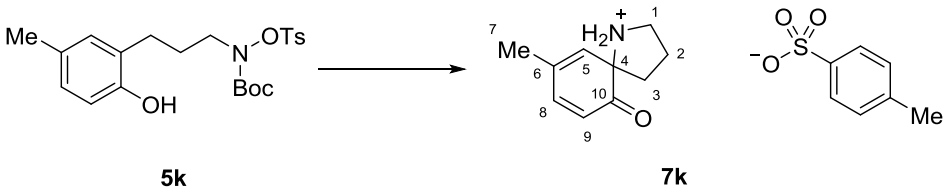
***tert*-Butyl (3-(2-hydroxy-5-methylphenyl)propyl)(tosyloxy)carbamate (5k)**



5k

General procedure D: *tert*-Butyl (3-(2-((*tert*-butyldimethylsilyl)oxy)-5-methylphenyl)propyl) (tosyloxy)carbamate (0.44 g, 0.80 mmol) and 1:1 TBAF/AcOH solution (0.1 M in THF, 0.80 mmol) in THF (16 mL) were employed. Purification by flash column chromatography (gradient, eluent 20 – 33 % EtOAc/hexane) afforded **5k** (0.27 g, 77%) as a colorless solid; m.p.: 107 - 108 ºC (EtOAc/hexane); R_f = 0.2 (20 % EtOAc/hexane); ν_{max} / cm^{-1} (solid) 3447 (m), 2986 (m), 1685 (s), 1509 (m), 1382 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (2H, d, *J* = 8.3 Hz, Ts ArC<u>H</u>), 7.33 (2H, d, *J* = 8.1 Hz, Ts ArC<u>H</u>), 7.03 - 6.81 (2H, m, C**8**-<u>H</u>, C**9**-<u>H</u>), 6.64 (1H, d, *J* = 8.0 Hz, C**5**-<u>H</u>), 4.99 (1H, s, O<u>H</u>), 3.65 (2H, br s, C**1**-<u>H_2</u>), 2.56 (2H, t, *J* = 7.8 Hz, C**3**-<u>H_2</u>), 2.44 (3H, s, Ts C<u>H_3</u>), 2.24 (3H, s, C**7**-<u>H_3</u>), 2.0 - 1.89 (2H, m, C**2**-<u>H_2</u>), 1.21 (9H, s, Boc (C<u>H_3</u>)$_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.8 (C=O), 151.4 (C**10**), 145.7 (Ts Ar<u>C</u>), 131.3 (Ts Ar<u>C</u>), 130.8 (C**5**), 129.9 (C**6**) 129.8 (2 × Ts Ar<u>C</u>H), 129.6 (2 × Ts Ar<u>C</u>H), 127.8 (C**8**), 127.0 (C**4**), 115.4 (C**9**), 83.5 (Boc <u>C</u>(CH$_3$)$_3$), 53.0 (C**1**), 27.7 (Boc (<u>C</u>H$_3$)$_3$), 27.2 (C**3**), 26.3 (C**2**), 21.8 (Ts <u>C</u>H$_3$), 20.6 (C**7**); HRMS (ESI^+) Calculated for $C_{22}H_{29}NNaO_6S$: 458.1608. Found $[M+Na]^+$: 458.1608.

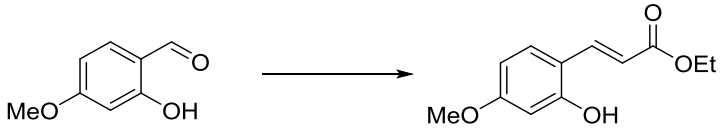
9-Methyl-1-azaspiro[4.5]deca-7,9-dien-6-one tosylate (7k)



5k **7k**

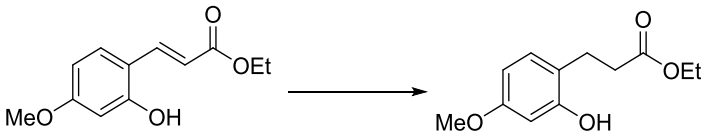
General procedure E: *tert*-Butyl (3-(2-hydroxy-5-methylphenyl)propyl)(tosyloxy)carbamate (**5k**) (25.2 mg, 0.06 mmol) and TFA (8.9 μL, 0.12 mmol) in anhydrous TFE (0.57 mL) were employed. Upon completion, the reaction mixture was concentrated *in vacuo* to afford **7k** as a brown solid. *An in situ yield was obtained by ^{1}H NMR against 1,4-dinitrobenzene as an internal standard; a yield of 91% was obtained*. R_f = 0.1 (5 % MeOH/CH_2Cl_2); ν_{max} / cm^{-1} (solid) 3447 (m, br), 2970 (m), 2923 (m), 1673 (m), 1655 (m), 1606 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.31 (1H, br s, NH), 8.16 (1H, br s, NH), 7.71 (2H, d, *J* = 8.0 Hz, Ts ArCH), 7.18 (2H, d, *J* = 7.9 Hz, Ts ArCH), 6.83 (1H, dd, *J* = 10.0, 2.2 Hz, C**8**-H), 6.34 (1H, br s, C**5**-H), 6.07 (1H, d, *J* = 10 Hz, C**9**-H), 3.72 (2H, br s, C**1**-H_2), 2.36 (3H, s, Ts CH_3), 2.24 - 2.05 (4H, m, C**2**-H_2, C**3**-H_2), 1.83 (3H, s, C**7**-H_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.6 (C**10**), 147.1 (C**8**), 141.3 (Ts ArC), 140.4 (Ts ArC), 132.6 (C**6**), 131.4 (C**5**), 129.2 (Ts ArCH), 126.0 (Ts ArCH), 123.9 (C**9**), 72.5 (C**4**), 48.2 (C**1**), 37.2 (C**2**/C**3**), 22.6 (C**2**/C**3**), 21.5 (Ts CH_3), 20.9 (C**7**); HRMS (ESI$^+$) Calculated for $C_{10}H_{14}NO$: 164.1070. Found $[M]^+$: 164.1071.

Ethyl (*E*)-3-(2-hydroxy-4-methoxyphenyl)acrylate[19]



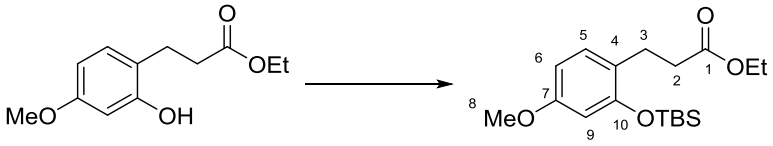
General procedure F: 2-Hydroxy-4-methoxybenzaldehyde (1.80 g, 12.0 mmol) and ethyl 2-(triphenyl-phosphaneylidene) acetate (6.27 g, 18.0 mmol) in CH_2Cl_2 (15 mL) were employed. Purification by flash column chromatography (20 % EtOAc/hexane) afforded the title compound (2.73 g, quant.) as a colorless solid; R_f = 0.3 (20 % EtOAc/hexane); ^{1}H NMR (400 MHz, $(CD_3)_2CO$) δ 9.13 (1H, s), 7.93 (1H, d, *J* = 16.1 Hz), 7.54 (1H, d, *J* = 8.4 Hz), 6.53 - 6.50 (2H, m), 6.48 (1H, d, *J* = 16.1 Hz), 4.18 (2H, q, *J* = 7.1 Hz), 3.79 (3H, s), 1.27 (3H, t, *J* = 7.1 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.0, 163.6, 158.9, 140.7, 131.2, 116.1, 115.6, 107.2, 102.3, 60.4, 55.7, 14.8. *Spectroscopic properties were consistent with the data available in the literature*.[19]

Ethyl 3-(2-hydroxy-4-methoxyphenyl)propanoate[20]



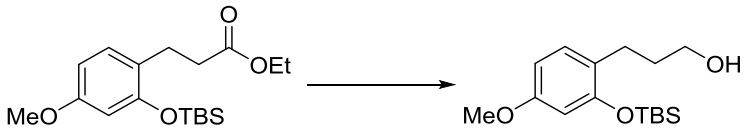
General procedure G: Ethyl (*E*)-3-(2-hydroxy-4-methoxyphenyl)acrylate (2.22 g, 10.0 mmol) and 10 wt.% Pd/C (5 mol%) in EtOH (30 mL) were employed to afford the title compound (2.21 g, 99 %) as an off-white solid; R_f = 0.2 (20 % EtOAc/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (1H, s), 6.97 (1H, d, *J* = 8.3 Hz), 6.48 - 6.40 (2H, m), 4.14 (2H, q, *J* = 7.2 Hz), 3.75 (3H, s), 2.79 - 2.89 (2H, m), 2.63 - 2.73 (2H, m), 1.24 (3H, t, *J* = 7.2 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.1, 159.7, 155.4, 131.1, 119.7, 106.9, 102.9, 61.5, 55.4, 35.6, 24.1, 14.2. *Spectroscopic properties were consistent with the data available in the literature*.[20]

Ethyl 3-(2-((*tert*-butyldimethylsilyl)oxy)-4-methoxyphenyl)propanoate



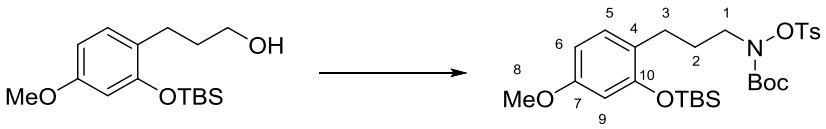
Ethyl 3-(2-hydroxy-4-methoxyphenyl)propanoate (1.68 g, 7.50 mmol), *tert*-butyldimethylsilyl chloride (1.36 g, 9.00 mmol), and imidazole (1.28 g, 18.75 mmol) in DMF (15 mL) were employed. Purification by flash column chromatography (20 % EtOAc/pentane) afforded the title compound (1.59 g, 63 %) as a colorless oil; R_f = 0.5 (20 % EtOAc/hexane); ν_{max} / cm^{-1} (film) 2955 (m), 2931 (m), 2858 (m), 1733 (s), 1611 (s), 1505 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04 (1H, d, *J* = 8.3 Hz, C**5**-H), 6.44 (1H, dd, *J* = 8.3, 2.5 Hz, C**6**-H), 6.38 (1H, d, *J* = 2.5 Hz, C**9**-H), 4.12 (2H, q, *J* = 7.1 Hz, OCH_2), 3.75 (3H, s, C**8**-H_3), 2.84 (2H, dd, *J* = 8.9, 7.0 Hz, C**3**-H_2), 2.54 (2H, dd, *J* = 8.9, 7.0 Hz, C**2**-H_2), 1.23 (3H, t, *J* = 7.1 Hz, CH_2CH_3), 1.02 (9H, s, TBS $(CH_3)_3$), 0.25 (6H, s, TBS $Si(CH_3)_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.4 (C=O), 159.1 (C**7**), 154.5 (C**10**), 130.4 (C**5**), 123.7 (C**4**), 105.7 (C**6**/C**9**), 105.6 (C**6**/C**9**), 60.3 (OCH_2), 55.4 (C**8**), 34.9 (C**2**), 25.9 (TBS $(CH_3)_3$), 25.8 (C**3**), 18.3 (TBS $SiC(CH_3)_3$), 14.4 (CH_2CH_3), -4.0 (TBS $Si(CH_3)_2$); HRMS (ESI^+) Calculated for $C_{18}H_{30}NaO_4Si$: 361.1806. Found $[M+Na]^+$: 361.1820.

3-(2-((*tert*-Butyldimethylsilyl)oxy)-4-methoxyphenyl)propan-1-ol[21]



A solution of ethyl 3-(2-((*tert*-butyldimethylsilyl)oxy)-4-methoxyphenyl)propanoate (1.01 g, 3.0 mmol) in anhydrous THF (15 mL) was cooled to -78 °C before 2.0 eq. DIBALH (1 M in CH_2Cl_2) was added dropwise to maintain the temperature of the reaction mixture below -75 °C. The reaction was stirred at this temperature for 4 h and then warmed to 0 °C and stirred for an additional 2 h. The reaction mixture was diluted with EtOAc (10 mL) and quenched with Rochelle's salt (10 mL). The mixture was filtered through Celite® and washed with EtOAc. The phases were separated and the aqueous phase extracted with EtOAc (10 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated *in vacuo*. Purification by flash column chromatography (33 % EtOAc/hexane) afforded the title compound (0.44 g, 50 %) as a colorless oil; R_f = 0.3 (33 % EtOAc/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03 (1H, d, *J* = 8.4 Hz), 6.47 (1H, dd, *J* = 8.4, 2.4 Hz), 6.39 (1H, d, *J* = 2.4 Hz), 3.76 (3H, s), 3.61 (2H, t, *J* = 6.4 Hz), 2.62 (2H, t, *J* = 7.2 Hz), 1.85 - 1.77 (2H, m), 1.64 (1H, br s), 1.01 (9H, s), 0.25 (6H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.8, 154.4, 130.6, 124.7, 106.1, 105.7, 62.4, 55.4, 33.4, 25.9, 25.8, 18.4, -4.0. *Spectroscopic properties were consistent with the data available in the literature*.[21]

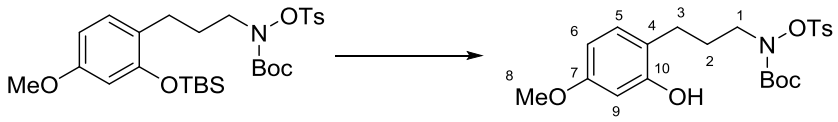
***tert*-Butyl (3-(2-((*tert*-butyldimethylsilyl)oxy)-4-methoxyphenyl)propyl)(tosyloxy) carbamate**



General procedure C: 3-(2-((*tert*-Butyldimethylsilyl)oxy)-4-methoxyphenyl)propan-1-ol (0.44 g, 1.50 mmol), PPh_3 (0.47 g, 1.80 mmol), DIAD (0.35 mL, 1.80 mmol) and TsONHBoc (0.52 g, 1.80 mmol) in anhydrous THF (6 mL) were employed. Purification by flash column chromatography (10% EtOAc/hexane) afforded the title compound (0.82 g, 96 %) as a colorless oil; R_f = 0.5 (33 % EtOAc/hexane); ν_{max} / cm^{-1} (film) 2955 (m), 2931 (m), 1720 (s), 1504 (s), 1160 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (2H, d, *J* = 8.3 Hz, Ts ArC<u>H</u>), 7.31 (2H, d, *J* = 8.3 Hz, Ts ArC<u>H</u>), 7.00 (1H, d, *J* = 8.3 Hz, C**5**-<u>H</u>), 6.44 (1H, dd, *J* = 8.3, 2.5 Hz, C**6**-<u>H</u>), 6.36 (1H, d, *J* = 2.5 Hz, C**9**-<u>H</u>), 3.75 (3H, s, C**8**-<u>H</u>$_3$), 3.71 - 3.49 (2H, m, C**1**-<u>H</u>$_2$), 2.49 (2H, t, *J* = 7.7

Hz, C**3**-$\underline{H}_2$), 2.43 (3H, s, Ts C$\underline{H}_3$), 1.95 - 1.81 (2H, m, C**2**-$\underline{H}_2$), 1.21 (9H, s, Boc (C$\underline{H}_3$)$_3$), 1.01 (9H, s, TBS (C$\underline{H}_3$)$_3$), 0.24 (6H, s, TBS Si(C$\underline{H}_3$)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.8 (C**7**), 155.5 (C=O), 154.3 (C**10**), 145.6 (Ts Ar$\underline{C}$), 131.4 (Ts Ar$\underline{C}$), 130.3 (C**5**), 129.7 (2 × Ts Ar$\underline{C}$H), 129.6 (2 × Ts Ar$\underline{C}$H), 124.1 (C**4**), 105.7 (C**6**), 105.5 (C**9**), 83.1 (Boc $\underline{C}$(CH$_3$)$_3$), 55.3 (C**8**), 52.8 (C**1**), 27.7 (Boc ($\underline{C}$H$_3$)$_3$), 27.0 (C**3**), 26.2 (C**2**), 25.9 (TBS ($\underline{C}$H$_3$)$_3$), 21.8 (Ts $\underline{C}$H$_3$), 18.3 (TBS Si$\underline{C}$(CH$_3$)$_3$), -4.1 (TBS Si($\underline{C}$H$_3$)$_2$); HRMS (ESI$^+$) Calculated for $C_{28}H_{43}NNaO_7SSi$: 588.2422. Found [M+Na]$^+$: 588.2426.

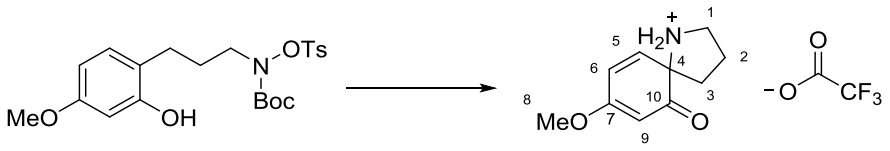
***tert*-Butyl (3-(2-hydroxy-4-methoxyphenyl)propyl)(tosyloxy)carbamate (5l)**



5l

General procedure D: *tert*-Butyl (3-(2-((*tert*-butyldimethylsilyl)oxy)-4-methoxyphenyl)propyl) (tosyloxy)carbamate (0.56 g, 1.00 mmol) and 1:1 TBAF/AcOH solution (0.1 M in THF, 0.1 mmol) in THF (20 mL) were employed. Purification by flash column chromatography (33 % EtOAc/hexane) afforded **5l** (0.30 g, 68 %) as a colorless, viscous oil; R_f = 0.2 (33 % EtOAc/hexane); ν_{max} / cm^{-1} (film) 3422 (br s), 2936 (m), 1720 (m), 1508 (m), 1368 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (2H, d, *J* = 8.0 Hz, Ts ArC$\underline{H}$), 7.33 (2H, d, *J* = 8.0 Hz, Ts ArC$\underline{H}$), 6.98 (1H, d, *J* =8.3 Hz, C**5**-$\underline{H}$), 6.42 (1H, dd, *J* = 8.3, 2.4 Hz, C**6**-$\underline{H}$), 6.36 (1H, d, *J* = 2.4 Hz, C**9**-$\underline{H}$), 5.37 (1H, br s, O$\underline{H}$), 3.75 (3H, s, C**8**-$\underline{H}_3$), 3.72 - 3.53 (2H, m, C**1**-$\underline{H}_2$), 2.54 (2H, t, *J* = 7.7 Hz, C**3**-$\underline{H}_2$), 2.44 (3H, s, Ts C$\underline{H}_3$), 1.98 - 1.85 (2H, m, C**2**-$\underline{H}_2$), 1.22 (9H, s, Boc (C$\underline{H}_3$)$_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.3 (C**7**), 156.0 (C=O), 154.6 (C**10**), 145.9 (Ts Ar$\underline{C}$), 131.4 (Ts Ar$\underline{C}$), 130.7 (C**5**), 130.0 (2 × Ts Ar$\underline{C}$H), 129.7 (2 × Ts Ar$\underline{C}$H), 119.6 (C**4**), 106.1 (C**6**), 102.1 (C**9**), 83.6, 55.5 (C**8**), 53.0 (C**1**), 27.8 (Boc ($\underline{C}$H$_3$)$_3$), 26.6 (C**2**/C**3**), 26.5 (C**2**/C**3**), 21.8 (Ts $\underline{C}$H$_3$); HRMS (ESI$^+$) Calculated for $C_{22}H_{29}NNaO_7S$: 474.1557. Found [M+Na]$^+$: 474.1560.

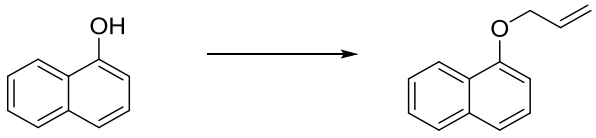
8-Methoxy-1-azaspiro[4.5]deca-7,9-dien-6-one trifluoroacetate (7l)



5l **7l**

General procedure E: *tert*-Butyl (3-(2-hydroxy-4-methoxyphenyl)propyl)(tosyloxy) carbamate (**5l**) (67.7 mg, 0.15 mmol) and TFA (23 μL, 0.30 mmol) in TFE (1.5 mL) were stirred at r.t. for 25 h. Purification by flash column chromatography (EtOAc) afforded **7l** (34.1 mg, 78 %) as a yellow oil; R_f = 0.1 (5 % MeOH/CH_2Cl_2); ν_{max} / cm^{-1} (film) 2987 (m), 2901 (m), 1672 (s), 1634 (m); ^{1}H NMR (400 MHz, CD_3OD) δ 6.69 (1H, d, *J* = 10.1 Hz, C**5**-H), 6.36 (1H, dd, *J* = 10.1, 2.2 Hz, C**6**-H), 5.63 (1H, d, *J* = 2.2 Hz, C**9**-H), 3.88 (3H, s, C**8**-H_3), 3.69 - 3.54 (2H, m, C**1**-H_2), 2.32 - 2.16 (4H, m, C**2**-H_2, C**3**-H_2). *The signals corresponding to the NH_2 were not observed.* ^{13}C NMR (101 MHz, CD_3OD) δ 196.9 (C**10**), 173.1 (C**7**), 138.5 (C**5**), 125.5 (C**6**), 98.8 (C**9**), 71.4 (C**4**), 57.5 (C**8**), 48.5 (C**1**), 39.4 (C**3**), 24.2 (C**2**). *The signals corresponding to the trifluoroacetate group could not be resolved due to their weak intensity*. HRMS (ESI^+) Calculated for $C_{10}H_{14}NO_2$: 180.1019. Found $[M+H]^+$: 180.1011.

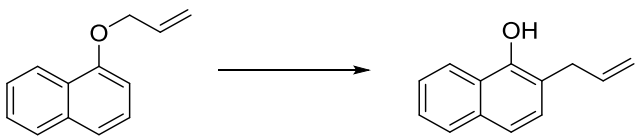
1-(Allyloxy)naphthalene[22]



The title compound was prepared according to a literature procedure.[22]

Spectroscopic properties were consistent with the data available in the literature.[23]

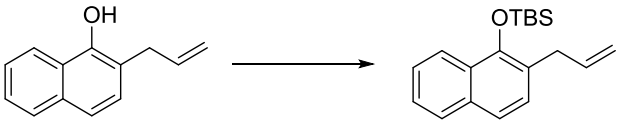
2-Allylnaphthalen-1-ol[24]



The title compound was prepared according to a literature procedure.[22]

Spectroscopic properties were consistent with the data available in the literature.[24]

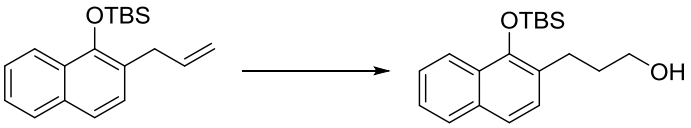
((2-Allylnaphthalen-1-yl)oxy)(*tert*-butyl)dimethylsilane[24]



The title compound was prepared according to a literature procedure.[22]

S*pectroscopic properties were consistent with the data available in the literature*.[24]

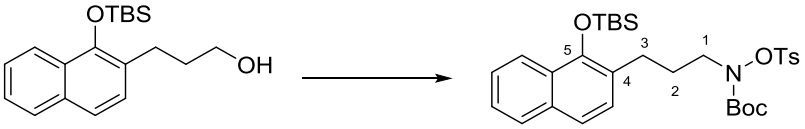
3-(1-((*tert*-Butyldimethylsilyl)oxy)naphthalen-2-yl)propan-1-ol[22]



The title compound was prepared according to a literature procedure.[22]

Spectroscopic properties were consistent with the data available in the literature.[22]

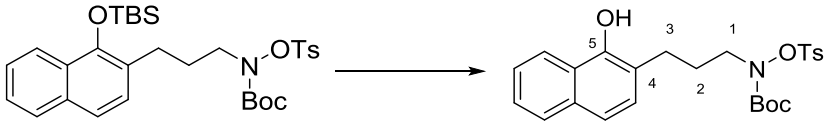
***tert*-Butyl (3-(1-((*tert*-butyldimethylsilyl)oxy)naphthalen-2-yl)propyl)(tosyloxy) carbamate**



General procedure C: 3-(1-((*tert*-Butyldimethylsilyl)oxy)naphthalen-2-yl)propan-1-ol (0.47 g, 1.50 mmol), PPh_3 (0.47 g, 1.80 mmol), DIAD (0.35 mL, 1.80 mmol) and TsONHBoc (0.52 g, 1.80 mmol) in anhydrous THF (8 mL) were employed. Purification by flash column chromatography (10 % EtOAc/hexane) afforded the title compound as a colorless, viscous oil (0.67 g, 76 %); R_f = 0.4 (20 % EtOAc/hexane); ν_{max} / cm^{-1} (film) 2955 (m), 2930 (m), 2895 (m), 2858 (m), 1720 (s), 1382 (s), 1369 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 - 8.02 (1H, m, ArC<u>H</u>), 7.80 (2H, d, *J* = 8.4 Hz, Ts ArC<u>H</u>), 7.78 - 7.74 (1H, m, ArC<u>H</u>), 7.46 - 7.37 (3H, m, ArC<u>H</u>), 7.28 - 7.22 (3H, m, Ts ArC<u>H</u>, ArC<u>H</u>), 3.71 - 3.43 (2H, m, C**1**-<u>H</u>$_2$), 2.73 (2H, t, *J* = 7.7 Hz, C**3**-<u>H</u>$_2$), 2.39 (3H, s, Ts C<u>H</u>$_3$), 1.99 - 1.88 (2H, m, C**2**-<u>H</u>$_2$), 1.19 (9H, s, Boc (C<u>H</u>$_3$)$_3$), 1.11 (9H, s, TBS (C<u>H</u>$_3$)$_3$), 0.17 (6H, s, TBS Si(C<u>H</u>$_3$)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.6 (C=O),

148.3 (C**5**), 145.7 (Ts ArC), 133.8 (ArC), 131.4 (Ts ArC), 129.7 (2 × Ts ArCH) 129.6 (2 × Ts ArCH), 128.2 (ArC), 128.1 (ArCH), 127.7 (ArCH), 126.2 (C**4**), 125.4 (ArCH), 124.9 (ArCH), 123.2 (ArCH), 121.8 (ArCH), 83.3 (Boc C(CH$_3$)$_3$), 52.8 (C**1**), 27.7 (Boc (CH$_3$)$_3$), 27.6 (C**3**), 26.4 (C**2**), 26.3 (TBS (CH$_3$)$_3$), 21.8 (Ts CH$_3$), 18.9 (TBS SiC(CH$_3$)$_3$), -3.0 (TBS Si(CH$_3$)$_2$); HRMS (ESI$^+$) Calculated for $C_{31}H_{43}NNaO_6SSi$: 608.2472. Found [M+Na]$^+$: 608.2466.

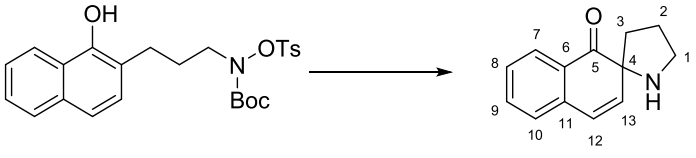
***tert*-Butyl (3-(1-hydroxynaphthalen-2-yl)propyl)(tosyloxy)carbamate (5m)**



5m

General procedure D: *tert*-Butyl (3-(1-((*tert*-butyldimethylsilyl)oxy)naphthalen-2-yl)propyl) (tosyloxy)carbamate (0.56 g, 0.97 mmol) and 1:1 TBAF/AcOH solution (0.1 M in THF, 0.97 mmol) in THF (20 mL) were employed. Purification by flash column chromatography (20 % EtOAc/hexane) afforded **5m** (0.31 g, 68 %) as a pale yellow solid; m.p.: 107 - 109 ^{o}C (EtOAc/hexane); R_f = 0.2 (20 % EtOAc/hexane); ν_{max} / cm^{-1} (solid) 3485 (m), 2970 (m), 2942 (m), 2882 (m), 1729 (s), 1385 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 - 8.15 (1H, m, ArCH), 7.85 (2H, d, *J* = 8.3 Hz, Ts ArCH), 7.77 (1H, dd, *J* = 8.1, 1.4 Hz, ArCH), 7.49 - 7.41 (2H, m, ArCH), 7.39 (1H, d, *J* = 8.4 Hz, ArCH), 7.30 (2H, d, *J* = 8.3 Hz, Ts ArCH), 7.22 (1H, d, *J* = 8.4 Hz, ArCH), 6.07 (1H, br s, OH), 3.69 (2H, t, *J* = 6.5 Hz, C**1**-H$_2$), 2.81 (2H, t, *J* = 7.5 Hz, C**3**-H$_2$), 2.43 (3H, s, Ts CH$_3$), 2.10-2.00 (2H, m, C**2**-H$_2$), 1.24 (9H, s, Boc (CH$_3$)$_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.4 (C=O), 148.8 (C**5**), 146.0 (Ts ArC), 133.6 (ArC), 131.3 (Ts ArC), 129.8 (2 × Ts ArCH), 129.7 (2 × Ts ArCH), 128.8 (ArCH), 127.7 (ArCH), 125.7 (ArCH), 125.4 (ArCH), 125.0 (ArC), 121.5 (ArCH), 120.5 (ArCH), 120.3 (ArC), 84.0 (Boc C(CH$_3$)$_3$), 52.9 (C**1**), 27.7 (Boc (CH$_3$)$_3$), 27.3 (C**3**), 27.2 (C**2**), 21.8 (Ts CH$_3$); HRMS (ESI$^+$) Calculated for $C_{25}H_{29}NNaO_6S$: 494.1607. Found [M+Na]$^+$: 494.1614.

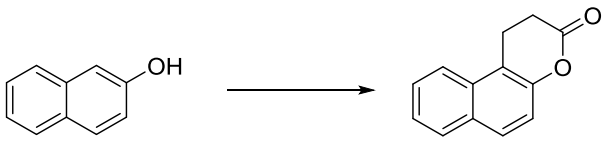
1*H*-spiro[naphthalene-2,2'-pyrrolidin]-1-one (7m)



5m **7m**

General procedure E: *tert*-Butyl (3-(1-hydroxynaphthalen-2-yl)propyl)(tosyloxy)carbamate (**5m**) (70.7 mg, 0.15 mmol) and TFA (23 μL, 0.3 mmol) in 30:1 anhydrous TFE/CH_2Cl_2 (1.5 mL) were stirred at r.t. for 26 h. Purification by flash column chromatography (gradient eluent 50 % EtOAc/hexane – 100 % EtOAc) afforded **7m** (11.4 mg, 38 %) as a yellow/brown solid; m.p.: 57 - 60 °C (EtOAc/hexane); R_f = 0.1 (EtOAc); ν_{max} / cm^{-1} (solid) 2920 (m), 2851 (m), 1674 (s), 1595 (s), 1371 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (1H, d, *J* = 7.7 Hz, C**7**-H), 7.56 - 7.51 (1H, m, C**9**-H), 7.34 - 7.29 (1H, m, C**8**-H), 7.17 (1H, d, *J* = 7.5 Hz, C**10**-H), 6.43 (1H, d, *J* = 10.0 Hz, C**12**-H), 6.25 (1H, d, *J* = 10.0 Hz, C**13**-H), 3.41 - 3.33 (1H, m, C**1**-H), 3.13 - 3.05 (1H, m, C**1**-H'), 2.40 (1H, br s, NH), 2.11 - 2.06 (1H, m, C**3**-H), 1.92 - 1.78 (3H, m, C**3**-H', C**2**-H_2); ^{13}C NMR (101 MHz, $CDCl_3$) δ 203.7 (C**5**), 139.8 (C**13**), 138.2 (C**11**), 134.7 (C**9**), 129.0 (C**6**), 127.9 (C**8**), 127.3 (C**7**), 127.2 (C**10**), 123.3 (C**12**), 70.2 (C**4**), 48.4 (C**1**), 38.9 (C**3**), 25.9 (C**2**); HRMS (ESI^+) Calculated for $C_{13}H_{14}NO$: 200.1069. Found $[M+H]^+$: 200.1079.

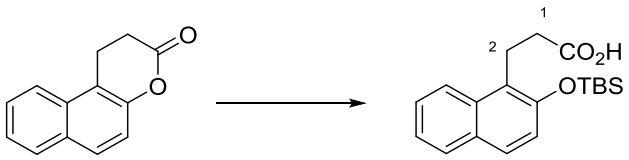
1,2-Dihydro-3*H*-naphtho[2,1-b]pyran-3-one[25]



The compound was prepared according to a literature procedure.[25]

Spectroscopic properties were consistent with the data available in the literature.[25]

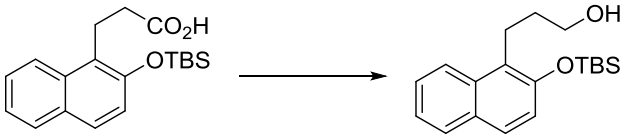
3-(2-((*tert*-Butyldimethylsilyl)oxy)naphthalen-1-yl)propanoic acid



To a solution of 1,2-Dihydro-3H-naphtho[2,1-b]pyran-3-one (7.90 g, 37.0 mmol) in THF (200 mL) was added aq. 1 M LiOH (125 mL). After stirring at r.t. overnight the pH was acidified to approx. 3 with 1 M HCl. The product was extracted with EtOAc (50 mL), dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was dissolved in DMF (20 mL) and *tert*-butyldimethylsilyl chloride (12.2 g, 81.4 mmol) and imidazole (8.30 g, 122.1 mmol) were added at 0 °C. After being stirred at r.t. overnight the reaction was quenched by addition of H_2O and the product was extracted with hexane, dried over $MgSO_4$, filtered and concentrated

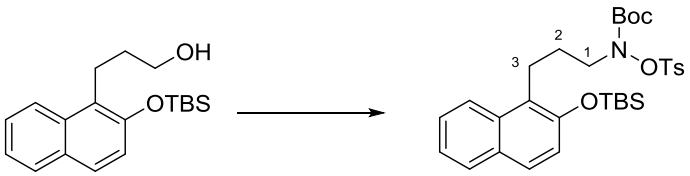
in vacuo. To the crude product in MeOH (30 mL) and THF (30 mL) was added aq. K_2CO_3 (74.0 mmol, 10.2 g in 100 mL H_2O). After stirring for 5 h the reaction was quenched with aq. 1 M HCl (100 mL) at 0 °C. The mixture was extracted with Et_2O, dried over Na_2SO_4, filtered and concentrated *in vacuo*. Purification by flash column chromatography (20 % EtOAc/hexane) afforded the title compound (8.10 g, 66 %) as a pale yellow solid; m.p.: 94 - 96 °C (EtOAc/hexane); R_f = 0.3 (33 % EtOAc/hexane); ν_{max} / cm^{-1} (solid) 2957 (m), 2928 (m), 2900 (m), 2857 (m), 1699 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (1H, d, *J* = 8.5 Hz, ArC<u>H</u>), 7.79 (1H, d, *J* = 7.8 Hz, ArC<u>H</u>), 7.65 (1H, d, *J* = 8.5 Hz, ArC<u>H</u>), 7.51 (1H, t, *J* = 7.7 Hz, ArC<u>H</u>), 7.36 (1H, t, *J* = 7.5 Hz, ArC<u>H</u>), 7.11 (1H, d, *J* = 8.9 Hz, ArC<u>H</u>), 3.43 (2H, t, *J* = 8.5 Hz, C**2**-<u>H</u>$_2$), 2.67 (2H, t, *J* = 8.5 Hz, C**3**-<u>H</u>$_2$), 1.08 (9H, s, TBS (C<u>H</u>$_3$)$_3$), 0.31 (6H, s, TBS Si(C<u>H</u>$_3$)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 179.3 (C=O), 150.8 (Ar<u>C</u>), 133.0 (Ar<u>C</u>), 129.5 (Ar<u>C</u>), 128.6 (Ar<u>C</u>H), 127.9 (Ar<u>C</u>H), 126.5 (Ar<u>C</u>H), 123.4 (Ar<u>C</u>H), 123.1 (Ar<u>C</u>), 122.8 (Ar<u>C</u>H), 120.2 (Ar<u>C</u>H), 33.9 (C**1**), 25.8 (TBS (<u>C</u>H$_3$)$_3$), 21.0 (C**2**), 18.3 (TBS Si<u>C</u>(CH$_3$)$_3$), 3.9 (TBS Si(<u>C</u>H$_3$)$_2$); HRMS (ESI$^+$) Calculated for $C_{19}H_{26}NaO_3Si$: 353.1543. Found $[M+Na]^+$: 353.1551.

3-(2-(*tert*-Butyldimethylsilyloxy)naphthalen-1-yl)propan-1-ol[22]



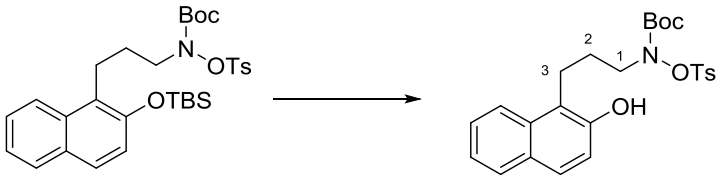
General procedure I: 3-(2-((*tert*-Butyldimethylsilyl)oxy)naphthalen-1-yl)propanoic acid (1.65 g, 5.00 mmol), Et_3N (0.70 mL, 5.00 mmol), ethyl chloroformate (0.54 g, 5.00 mmol) and $NaBH_4$ (0.47 g, 12.5 mmol) in THF (50 mL) and H_2O (20 mL) were employed. Purification by flash column chromatography (20 % EtOAc/hexane) afforded the title compound (1.19 g, 75 %) as a colorless oil; R_f = 0.6 (33 % EtOAc/hexane); ν_{max} / cm^{-1} : (film) 3336 (m, br), 2953 (m), 2929 (m), 2882 (m), 2857 (m), 1622 (m), 1594 (m), 1465 (m), 1264 (m), 1241 (s), ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (1H, d, *J* = 8.1 Hz), 7.79 (1H, d, *J* = 8.4 Hz), 7.63 (1H, d, *J* = 8.6 Hz), 7.48 (1H, t, *J* = 7.8 Hz), 7.35 (1H, t, *J* = 7.2 Hz), 7.12 (1H, d, *J* = 9.0 Hz), 3.63 (2H, t, *J* = 5.9 Hz), 3.20 (2H, t, *J* = 6.7 Hz), 2.53 (1H, br s), 1.95 (2H, qn, *J* = 7.4 Hz), 1.10 (9H, s), 0.31 (6H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.6, 133.4, 129.9, 128.6, 127.4, 126.3, 124.7, 123.6, 123.5, 120.6, 62.2, 32.5, 26.0, 21.5, 18.5, -3.8. *Spectroscopic properties were consistent with the data available in the literature*.[22]

***tert*-Butyl (3-(2-((*tert*-butyldimethylsilyl)oxy)naphthalen-1-yl)propyl) (tosyloxy) carbamate**



To a solution of 3-(2-(*tert*-butyldimethylsilyloxy)naphthalen-1-yl)propan-1-ol (0.63 g, 2.00 mmol), *tert*-butyl (tosyloxy)carbamate (0.56 g, 3.00 mmol) and PPh_3 (1.05 g, 4.00 mmol) in anhydrous PhMe:THF (3:1, 8 mL/mmol) at 0 °C was added a solution of DIAD (0.78 mL, 4.00 mmol) in anhydrous PhMe (2 mL/mmol) dropwise. The reaction was stirred at r.t. until completion by TLC analysis (4 h). The reaction mixture was concentrated *in vacuo* and purification by flash column chromatography (gradient 20 – 25 % EtOAc/hexane) afforded the title compound (0.74 g, 63 %) as a colorless solid; m.p.: 79 - 80 °C (EtOAc/hexane); R_f = 0.7 (33 % EtOAc/hexane); ν_{max} / cm^{-1} (solid) 2961 (m), 2927 (m), 2857 (m), 1709 (s), 1596 (m), 1466 (m), 1368 (s), 1240 (s), 1174 (s), 1164 (s), 1153 (s), 1087 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (1H, d, *J* = 8.6 Hz, ArC<u>H</u>), 7.82 (2H, d, *J* = 8.3 Hz, ArC<u>H</u>), 7.75 (1H, d, *J* = 8.2 Hz, ArC<u>H</u>), 7.59 (1H, d, *J* = 8.8 Hz, ArC<u>H</u>), 7.47 - 7.43 (1H, m, ArC<u>H</u>), 7.33 (1H, ddd, *J* = 8.1, 6.8, 1.1 Hz, ArC<u>H</u>), 7.27 (2H, d, *J* = 8.2 Hz, ArC<u>H</u>), 7.05 (1H, d, *J* = 8.8 Hz, ArC<u>H</u>), 3.71 (2H, br s, C**1**-<u>H_2</u>), 3.02 (2H, t, *J* = 7.9 Hz, C**3**-<u>H_2</u>), 2.42 (3H, s, Ts C<u>H_3</u>), 1.98 - 1.89 (2H, m, C**2**-<u>H_2</u>), 1.16 (9H, s, Boc (C<u>H_3</u>)$_3$), 1.07 (9H, s, TBS (C<u>H_3</u>)$_3$), 0.27 (6H, s, Si(C<u>H_3</u>)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.5 (C=O), 150.6 (Ar<u>C</u>), 145.6 (Ts Ar<u>C</u>), 133.3 (Ar<u>C</u>), 131.5 (Ts Ar<u>C</u>), 129.7 (2 × Ts Ar<u>C</u>H), 129.6 (Ar<u>C</u>), 129.5 (2 × Ts ArC<u>H</u>), 128.6 (Ar<u>C</u>H), 127.5 (Ar<u>C</u>H), 126.4 (Ar<u>C</u>H), 124.2 (Ar<u>C</u>), 123.3 (Ar<u>C</u>H), 123.2 (Ar<u>C</u>H), 120.3 (Ar<u>C</u>H), 83.1 (Boc <u>C</u>(CH$_3$)$_3$), 53.1 (C**1**), 27.6 (Boc (<u>C</u>H$_3$)$_3$), 26.1 (C**2**), 26.0 (TBS (C<u>H$_3$</u>)$_3$), 22.7 (C**3**), 21.8 (Ts <u>C</u>H$_3$), 18.4 (TBS <u>C</u>(CH$_3$)$_3$), -3.8 (TBS Si(<u>C</u>H$_3$)$_2$); HRMS (ESI^+) Calculated for $C_{31}H_{43}NNaO_6SSi$: 608.2473. Found $[M+Na]^+$: 608.2456.

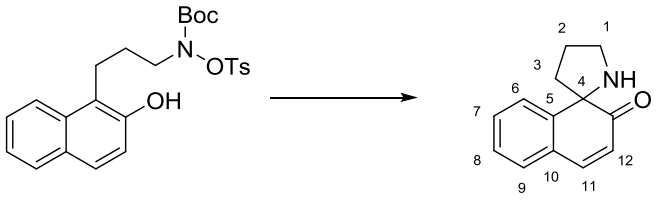
***tert*-butyl (3-(2-hydroxynaphthalen-1-yl)propyl)(tosyloxy)carbamate (5n)**



5n

General procedure D: *tert*-Butyl (3-(2-((*tert*-butyldimethylsilyl)oxy)naphthalen-1-yl)propyl)(tosyloxy) carbamate (0.16 g, 0.28 mmol) and 1:1 TBAF/AcOH solution (0.1 M in THF, 0.28 mmol) in THF were employed. Purification by flash column chromatography (33 % EtOAc/hexane) afforded **5n** (0.11 g, 84 %) as a pale yellow solid; m.p.: 55 - 57 ^{o}C (EtOAc/hexane); R_f = 0.35 (33 % EtOAc/hexane); ν_{max} / cm^{-1} 3359 (m, br), 2931 (m), 1721 (s), 1369 (s), 1191 (s), 1178 (s), 1154 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 - 7.83 (3H, m, Ts ArC<u>H</u>, ArC<u>H</u>), 7.77 (1H, d, *J* = 8.1 Hz, ArC<u>H</u>), 7.62 (1H, d, *J* = 8.8 Hz, ArC<u>H</u>), 7.47 (1H, ddd, *J* = 8.3, 6.9, 1.4 Hz, ArC<u>H</u>), 7.35 - 7.29 (3H, m, Ts ArC<u>H</u>, ArC<u>H</u>), 7.07 (1H, d, *J* = 8.8 Hz, ArC<u>H</u>), 5.60 (1H, br s, O<u>H</u>), 3.79 - 3.70 (2H, m, C**1**-<u>H_2</u>), 3.07 (2H, t, *J* = 7.8 Hz, C**3**-<u>H_2</u>), 2.44 (3H, s, Ts C<u>H_3</u>), 2.08 - 1.97 (2H, m, C**2**-<u>H_2</u>), 1.20 (9H, s, Boc (C<u>H_3</u>)$_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.1 (C=O), 151.1 (Ar<u>C</u>), 145.9 (Ts Ar<u>C</u>), 133.2 (Ar<u>C</u>), 131.3 (Ts Ar<u>C</u>), 129.7 (2 × Ts Ar<u>C</u>H), 129.7 (2 × Ts Ar<u>C</u>H), 129.5 (Ar<u>C</u>), 128.8 (Ar<u>C</u>H), 128.1 (ArC<u>H</u>), 126.6 (Ar<u>C</u>H), 123.1 (Ar<u>C</u>H), 122.8 (Ar<u>C</u>H), 118.8 (Ar<u>C</u>), 118.1 (ArC<u>H</u>), 83.6 (Boc <u>C</u>(CH$_3$)$_3$), 53.2 (C**1**), 27.7 (Boc (<u>C</u>H$_3$)$_3$), 26.4 (C**2**), 22.2 (C**3**) 21.8 (Ts <u>C</u>H$_3$); HRMS (ESI$^+$) Calculated for $C_{25}H_{29}NNaO_6S$: 494.1608. Found [M+Na]$^+$: 494.1598.

2*H*-spiro[naphthalene-1,2'-pyrrolidin]-2-one (7n)

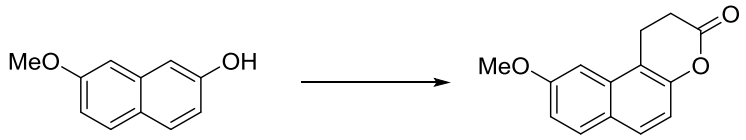


5n **7n**

General procedure E: *tert*-Butyl (3-(2-hydroxynaphthalen-1-yl)propyl)(tosyloxy)carbamate (**5n**) (117.9 mg, 0.25 mmol), TFA (38 µL, 0.50 mmol) and TFE (2.5 mL) were employed. After stirring at r.t. for 38 h, purification by flash column chromatography (50 % EtOAc/hexane) afforded **7n** (38.8 mg, 78 %) as a viscous yellow oil; R_f = 0.25 (33 % EtOAc/hexane); ν_{max}/ cm^{-1} (film) 3339 (m), 2965 (m), 2866 (m), 1671 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (1H, dd, *J* = 7.7, 0.9 Hz, C**6**-<u>H</u>), 7.41 - 7.34 (2H, m, C**11**-<u>H</u> and C**7**-<u>H</u>), 7.29 - 7.21 (2H, m, C**8**-<u>H</u> and C**9**-<u>H</u>), 6.17 (1H, d, *J* = 9.9 Hz, C**12**-<u>H</u>), 3.45 (1H, dt, *J* = 10.3, 6.4 Hz, C**1**-<u>H</u>), 3.28 (1H, dt, *J* = 10.2, 6.4 Hz, C**1**-<u>H</u>'), 2.34 - 2.22 (1H, m, C**3**-<u>H</u>), 1.96 - 1.69 (3H, m, C**2**-<u>H_2</u>, C**3**-<u>H</u>'); ^{13}C NMR (101 MHz, $CDCl_3$) δ 205.1, (C=O), 148.8 (C**5**), 144.8 (C**11**) , 130.1 (C**7**), 129.2

(C**8**), 129.1 (C**10**), 127.0 (C**9**), 126.0 (C**6**), 123.6 (C**12**), 73.9 (C**4**), 49.9 (C**1**), 42.9 (C**3**), 25.6 (C**2**); HRMS (ESI$^+$) Calculated for $C_{13}H_{13}NNaO$: 222.0889. Found $[M+Na]^+$: 222.0883.

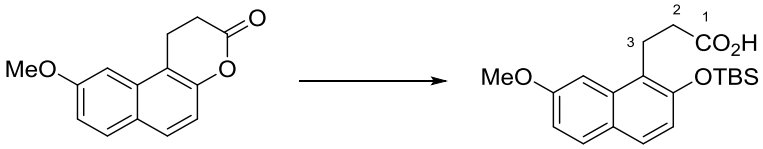
1,2-Dihydro-9-methoxy-3*H*-naphtho[2,1-b]pyran-3-one[26]



The title compound was prepared according to a literature procedure. [25]

Spectroscopic properties were consistent with the data available in the literature.[26]

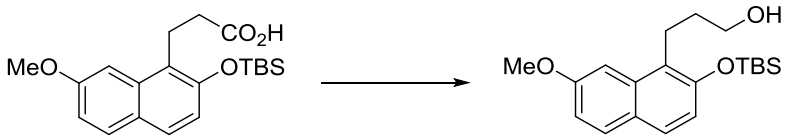
3-(2-((*tert*-Butyldimethylsilyl) oxy)-7-methoxynaphthalen-1-yl)propanoic acid



To a solution of 1,2-dihydro-9-methoxy-3*H*-naphtho[2,1-b]pyran-3-one (1.71 g, 7.50 mmol) in THF (75 mL) was added aq. 1 M LiOH (44.0 mL, 24.8 mmol). After stirring at r.t. overnight the pH was acidified to approx. 3 with aq. 1 M HCl. The product was extracted with EtOAc (50 mL), dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was dissolved in DMF (15 mL) and *tert*-butyldimethylsilyl chloride (2.50 g, 16.5 mmol) and imidazole (1.68 g, 24.8 mmol) were added at 0 ^{o} C. After being stirred at r.t. overnight the reaction was quenched by addition of H_2O and the product was extracted with hexane, dried over $MgSO_4$, filtered and concentrated *in vacuo*. To the crude product in MeOH (7.5 mL) and THF (7.5 mL) was added aq. K_2CO_3 (22 mL, 15.0 mmol). After stirring overnight at r.t., the reaction was quenched with aq. 1 M HCl (20 mL) at 0 ^{o}C. The organic phase was extracted with Et_2O (3 × 10 mL), dried over Na_2SO_4, filtered and concentrated *in vacuo*. Purification by flash column chromatography (20 % EtOAc/hexane) afforded the title compound (1.77 g, 65 %) as a yellow solid; m.p.: 113 - 115 ^{o}C (EtOAc/hexane); R_f = 0.5 (33 % EtOAc/hexane); ν_{max} / cm^{-1} (solid) 3675 (w), 2958 (m), 2927 (m), 1703 (s), 1627 (m), 1514 (s), 1264 (s), 1231 (s), 1037 (s); ^{1}H NMR ($CDCl_3$) δ 7.68 (1H, d, *J* = 8.9 Hz, ArC<u>H</u>), 7.56 (1H, d, *J* = 8.8 Hz, ArC<u>H</u>), 7.24 (1H, d, *J* = 2.4 Hz, ArC<u>H</u>), 7.02 (1H, dd, *J* = 8.9, 2.4 Hz, ArC<u>H</u>), 6.95 (1H, d, *J* = 8.8 Hz, ArC<u>H</u>), 3.95 (3H, s, OC<u>H</u>$_3$), 3.43 - 3.26 (2H, m, C**3**-<u>H</u>$_2$), 2.76 - 2.56 (2H, m, C**2**-<u>H</u>$_2$), 1.97 (9H, s, TBS (C<u>H</u>$_3$)$_3$), 0.29 (6H, s, TBS (Si(C<u>H</u>$_3$)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.9 (C=O),

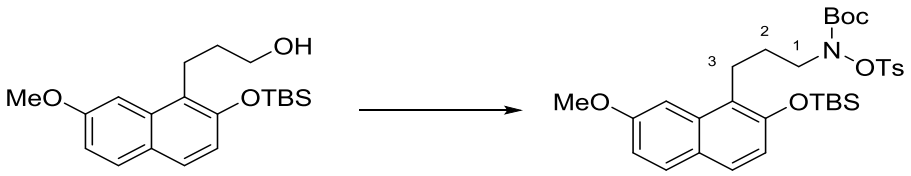
158.3 (Ar<u>C</u>), 151.4 (Ar<u>C</u>), 134.3 (Ar<u>C</u>), 130.1 (Ar<u>C</u>H), 127.6 (Ar<u>C</u>H), 124.8 (Ar<u>C</u>), 122.1 (Ar<u>C</u>), 117.6 (Ar<u>C</u>H), 115.7 (Ar<u>C</u>H), 101.7 (Ar<u>C</u>H), 55.3 (O<u>C</u>H$_3$), 33.5 (C**2**), 25.8 (TBS (<u>C</u>H$_3$)$_3$), 21.1 (C**3**), 18.3 (TBS Si<u>C</u>(CH$_3$)$_3$), -3.9 (TBS Si(<u>C</u>H$_3$)$_2$); HRMS (-ve ion) Calculated for $C_{20}H_{27}O_4Si$: 359.1684. Found $[M-H]^-$: 359.1685.

3-(2-((*tert*-Butyldimethylsilyl)oxy)-7-methoxynaphthalen-1-yl)propan-1-ol[22]



General procedure I: 3-(2-((*tert*-Butyldimethylsilyl)oxy)-7-methoxynaphthalen-1-yl)propanoic acid (1.08 g, 3.00 mmol), ethylchloroformate (0.29 mL, 3.00 mmol), Et$_3$N (0.42 mL, 3.00 mmol), and NaBH$_4$ (0.28 g, 7.50 mmol) were employed. Purification by flash column chromatography (20 % EtOAc/ hexane) afforded the title compound (0.68 g, 65 %) as a pale yellow oil; R_f = 0.25 (20 % EtOAc/hexane); ν_{max} / cm^{-1} (film) 3370 (br m), 2953 (m), 2930 (m), 2884 (m), 2857 (m), 1624 (s), 1513 (s), 1461 (s), 1230 (s); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.67 (1H, d, *J* = 8.9 Hz), 7.53 (1H, d, *J* = 8.8 Hz), 7.02 (1H, dd, *J* = 8.9, 2.4 Hz), 6.94 (1H, d, *J* = 8.8 Hz), 3.93 (3H, s), 3.59 (2H, t, *J* = 6.1 Hz), 3.14 (2H, t, *J* = 7.2 Hz), 2.06-1.77 (3H, m), 1.05 (9H, s), 0.27 (6H, s); ^{13}C NMR (101 MHz, CDCl$_3$) δ 158.0, 151.2, 134.5, 130.0, 127.0, 125.1, 123.4, 117.9, 115.6, 102.5, 62.0, 55.3, 31.9, 25.9, 21.5, 18.4, -3.9; HRMS (ESI$^+$) Calculated for $C_{20}H_{30}NaO_3Si$: 369.1856. Found $[M+Na]^+$: 369.1855. *Spectroscopic properties were consistent with the data available in the literature.*[22]

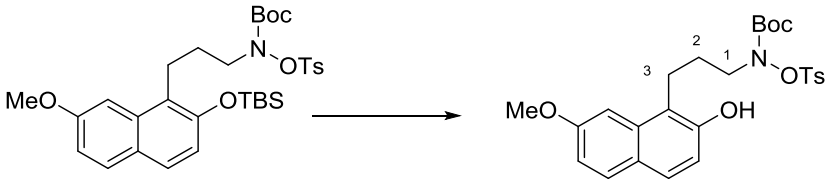
***tert*-Butyl (2-(2-((*tert*-butyldimethylsilyl)oxy)-7-methoxynaphthalen-1-yl)ethyl)(tosyloxy) carbamate**



General procedure C: 3-(2-((*tert*-Butyldimethylsilyl)oxy)-7-methoxynaphthalen-1-yl)propan-1-ol (0.40 g, 1.15 mmol), PPh$_3$ (0.36 g, 1.38 mmol), DIAD (0.27 mL, 1.38 mmol) and TsONHBoc (0.40 mg, 1.38 mmol) in anhydrous THF (5 mL) were employed. Purification by flash column chromatography (10 % EtOAc/hexane) afforded the title compound (0.48 g,

68 %) as a colorless oil; R_f = 0.5 (20 % EtOAc/hexane); ν_{max} / cm^{-1} (film) 2956 (m), 2930 (m), 2900 (m), 2859 (m), 1721 (s), 1623 (s), 1513 (s), 1381 (s), 1368 (s), 1231 (s), 1178 (s), 1152 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (2H, d, *J* = 8.2 Hz, Ts ArC<u>H</u>), 7.65 (1H, d, *J* = 8.9 Hz, ArC<u>H</u>), 7.51 (1H, d, *J* = 8.8 Hz, ArC<u>H</u>), 7.30 (2H, d, *J* = 8.1 Hz, Ts ArC<u>H</u>), 7.16 (1H, d, *J* = 2.4 Hz, ArC<u>H</u>), 7.00 (1H, dd, *J* = 8.9, 2.4 Hz, ArC<u>H</u>), 6.90 (1H, d, *J* = 8.8 Hz, ArC<u>H</u>), 3.96 (3H, s, OC<u>H</u>$_3$), 3.73 (2H, app. br s, C**1**-<u>H</u>$_2$), 2.96 (2H, t, *J* = 8.1 Hz, C**3**-<u>H</u>$_2$), 2.42 (3H, s, Ts, C<u>H</u>$_3$), 1.96 (2H, qn, *J* = 7.5 Hz, C**2**-<u>H</u>$_2$), 1.16 (9H, s, Boc (C<u>H</u>$_3$)$_3$), 1.05 (9H, s, TBS (C<u>H</u>$_3$)$_3$), 0.25 (6H, s, TBS (Si(C<u>H</u>$_3$)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.2 (Ar<u>C</u>), 155.4 (C=O), 151.2 (Ar<u>C</u>), 145.7 (Ts Ar<u>C</u>), 134.5 (Ar<u>C</u>), 131.4 (Ts Ar<u>C</u>), 13.0 (Ar<u>C</u>H), 129.7 (2 × Ts Ar<u>C</u>H), 129.6 (2 × Ts Ar<u>C</u>H), 127.2 (Ar<u>C</u>H), 124.9 (Ar<u>C</u>), 123.2 (Ar<u>C</u>), 117.7 (Ar<u>C</u>H), 116.0 (Ar<u>C</u>H), 101.9 (Ar<u>C</u>H), 83.2 (Boc <u>C</u>(CH$_3$)$_3$), 55.5 (O<u>C</u>H$_3$), 52.9 (C**1**), 27.6 (Boc (<u>C</u>H$_3$)$_3$), 26.0 (TBS (<u>C</u>H$_3$)$_3$), 25.8 (C**2**), 22.9 (C**3**), 21.8 (Ts <u>C</u>H$_3$), 18.4 (TBS <u>C</u>(CH$_3$)$_3$), -3.8 (TBS Si(<u>C</u>H$_3$)$_2$); HRMS (ESI$^+$) Calculate for $C_{32}H_{45}NNaO_7SSi$: 638.2578. Found $[M+Na]^+$: 638.2560.

***tert*-Butyl (3-(2-hydroxy-7-methoxynaphthalen-1-yl)propyl)(tosyloxy)carbamate (5o)**

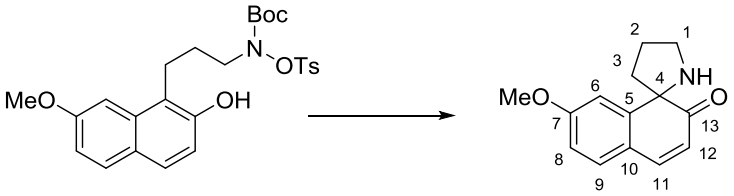


5o

General procedure D: *tert*-Butyl (2-(2-((*tert*-butyldimethylsilyl)oxy)-7-methoxynaphthalen-1-yl) ethyl)(tosyloxy)carbamate (0.30 g, 0.50 mmol) and 1:1 TBAF/AcOH solution (0.1 M in THF, 0.50 mmol) in THF (10 mL) were employed. Purification by flash column chromatography (gradient, eluent 20 – 33 % EtOAc/hexane) afforded **5o** (0.13 g, 51 %) as a pale yellow solid; R_f = 0.2 (20 % EtOAc/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (2H, d, *J* = 8.1 Hz, Ts ArC<u>H</u>), 7.65 (1H, d, *J* = 8.9 Hz, ArC<u>H</u>), 7.54 (1H, d, *J* = 8.7 Hz, ArC<u>H</u>), 7.32 (2H, d, *J* = 8.0 Hz, Ts ArC<u>H</u>), 7.14 (1H, d, *J* = 2.3 Hz, ArC<u>H</u>), 6.99 (1H, dd, *J* = 8.9, 2.4 Hz, ArC<u>H</u>), 6.89 (1H, d, *J* = 8.7 Hz, ArC<u>H</u>), 5.34 (1H, br s, O<u>H</u>), 3.95 (3H, s, OC<u>H</u>$_3$), 3.76 (2H, br s, C**1**-<u>H</u>$_2$), 3.00 (2H, t, *J* = 7.8 Hz, C**3**-<u>H</u>$_2$), 2.43 (3H, s, Ts C<u>H</u>$_3$), 2.07 - 2.00 (2H, m, C**2**-<u>H</u>$_2$), 1.19 (9H, s, Boc (C<u>H</u>$_3$)$_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.4 (Ar<u>C</u>), 155.9 (C=O), 151.3 (Ar<u>C</u>), 145.7 (Ts Ar<u>C</u>), 134.3 (Ar<u>C</u>), 131.2 (Ts Ar<u>C</u>), 130.1 (Ar<u>C</u>H) 129.6 (2 × Ts Ar<u>C</u>H), 129.5 (2 × Ts Ar<u>C</u>H), 127.7 (Ar<u>C</u>H), 124.7 (Ar<u>C</u>), 117.7 (Ar<u>C</u>H), 115.4 (Ar<u>C</u>H), 115.3 (Ar<u>C</u>H), 101.7 (Ar<u>C</u>H), 83.5 (Boc <u>C</u>(CH$_3$)$_3$), 55.3 (O<u>C</u>H$_3$), 52.9 (C**1**), 27.5 (Boc (<u>C</u>H$_3$)$_3$), 25.8

(C**2**), 22.2 (C**3**), 21.7 (Ts <u>C</u>H$_3$); HRMS (ESI$^+$) Calculated for $C_{26}H_{31}NNaO_7S$: 524.1713. Found [M+Na]$^+$: 524.1708.

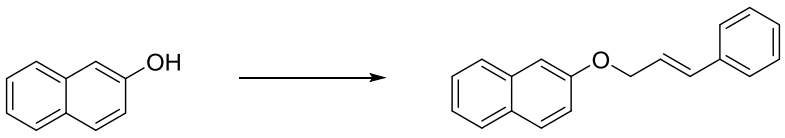
7-methoxy-2*H*-spiro[naphthalene-1,2'-pyrrolidin]-2-one (7o)



5o **7o**

General procedure E: *tert*-Butyl (3-(2-hydroxy-7-methoxynaphthalen-1-yl)propyl)(tosyloxy) carbamate (**5o**) (50.2 mg, 0.10 mmol), TFA (15 μL, 0.20 mmol) and TFE (1 mL) were employed. After stirring at r.t. for 48 h, purification by flash column chromatography (gradient, eluent 50 % EtOAc/hexane – EtOAc) afforded **7o** (17.4 mg, 76 %) as a yellow oil; R_f = 0.2 (EtOAc); ν_{max} / cm^{-1} (film) 3340 (m), 2963 (m), 2942 (m), 2865 (m), 1666 (s), 1601 (s), 1555 (m), 1279 (s), 1224 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (1H, d, *J* = 9.8 Hz, C**11**-<u>H</u>), 7.23 (1H, d, *J* = 2.6 Hz, C**6**-<u>H</u>), 7.19 (1H, d, *J* = 8.3 Hz, C**9**-<u>H</u>), 6.75 (1H, dd, *J* = 8.3, 2.6 Hz, C**8**-<u>H</u>), 6.03 (1H, d, *J* = 9.8 Hz, C**12**-<u>H</u>), 3.85 (3H, s, OC<u>H</u>$_3$), 3.44 (1H, dt, *J* = 10.2, 6.3 Hz, C**1**-<u>H</u>), 3.27 (1H, dt, *J* = 10.2, 6.3 Hz, C**1**-<u>H</u>'), 2.92 (1H, br s, N<u>H</u>), 2.30 - 2.23 (1H, m, C**3**-<u>H</u>), 1.93 - 1.72 (3H, m, C**3**-<u>H</u>' and C**2**-<u>H</u>$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 204.9 (C**13**), 161.5 (C**7**), 151.2 (C**5**), 144.7 (C**11**), 130.9 (C**9**), 122.4 (C**10**), 120.8 (C**12**), 112.2 (C**6**), 112.0 (C**8**), 74.1 (C**4**), 55.4 (<u>C</u>H$_3$), 49.9 (C**1**), 43.2 (C**3**), 25.1 (C**2**); HRMS (ESI$^+$) Calculated for $C_{14}H_{15}NNaO_2$: 252.0995. Found [M+Na]$^+$: 252.1002.

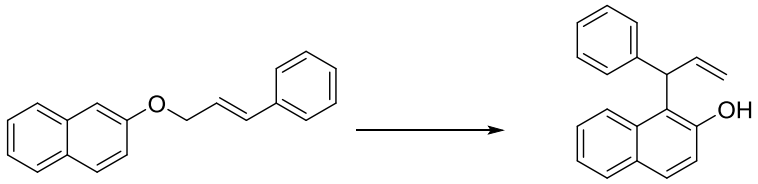
2-(Cinnamyloxy)naphthalene[27]



The title compound was prepared according to a literature procedure.[27]

Spectroscopic properties were consistent with the data available in the literature.[27]

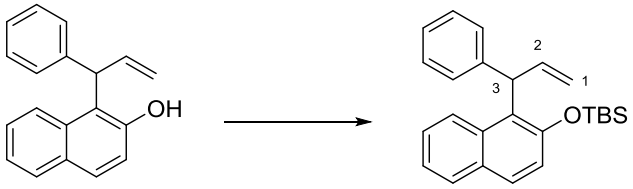
1-(1-Phenylallyl)naphthalen-2-ol[28]



The title compound was prepared according to a literature procedure.[27]

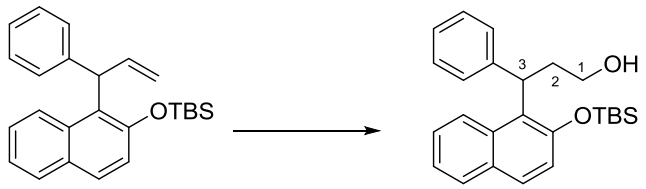
Spectroscopic properties were consistent with the data available in the literature.[28]

***tert*-Butyldimethyl((1-(1-phenylallyl)naphthalen-2-yl)oxy)silane**



To a solution of 1-(1-phenylallyl)naphthalen-2-ol (1.40 g, 5.30 mmol), in DMF (10 mL) was added *tert*-butyldimethylsilyl chloride (0.97 g, 6.45 mmol) and imidazole (0.91 g, 13.4 mmol) and the reaction mixture was stirred at r.t. overnight until completion by TLC analysis. The reaction was quenched with water (50 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The organic phase was washed with brine (20 mL), dried over Na_2SO_4, filtered and concentrated *in vacuo*. Purification by flash column chromatography (4% EtOAc/hexane) afforded the title compound (1.37 g, 69 %) as a pale-yellow oil; R_f = 0.4 (20 % EtOAc/hexane); ν_{max} / cm^{-1} (film) 2955 (m), 2928 (m), 1622 (m), 1586 (m), 1463 (m), 1253 (m), 1236 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (1H, d, *J* = 7.9 Hz, ArC<u>H</u>), 7.70 - 7.63 (2H, m, ArC<u>H</u>), 7.25 - 7.13 (8H, m, ArC<u>H</u>), 6.64 (1H, ddd, *J* = 17.3, 10.1, 7.5 Hz, C**2**-<u>H</u>), 5.91 (1H, d, *J* = 7.6 Hz, C**3**-<u>H</u>) 5.28 - 5.16 (2H, m, C**1**-<u>H</u>$_2$), 0.99 (9H, s, TBS (C<u>H</u>$_3$)$_3$), 0.23 (6H, d, *J* = 7.3 Hz, TBS Si(C<u>H</u>$_3$)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.4 (Ar<u>C</u>), 143.7 (Ar<u>C</u>), 138.9 (C**2**), 132.9 (Ar<u>C</u>), 130.4 (Ar<u>C</u>), 128.7 (Ar<u>C</u>H), 128.6 (Ar<u>C</u>H), 128.3 (2 × Ar<u>C</u>H), 127.6 (2 x Ar<u>C</u>H), 126.0 (Ar<u>C</u>), 125.7 (2 × Ar<u>C</u>H), 125.5 (Ar<u>C</u>H), 123.2 (Ar<u>C</u>H), 120.6 (Ar<u>C</u>H), 117.5 (C**1**), 45.4 (C**3**), 26.0 (TBS (<u>C</u>H$_3$)$_3$), 18.5 (TBS Si<u>C</u>(CH$_3$)$_3$), -3.6 (TBS Si(<u>C</u>H$_3$)$_2$); HRMS (ESI$^+$) Calculated for $C_{25}H_{31}NaOSi$: 397.1958. Found $[M+Na]^+$: 397.1972.

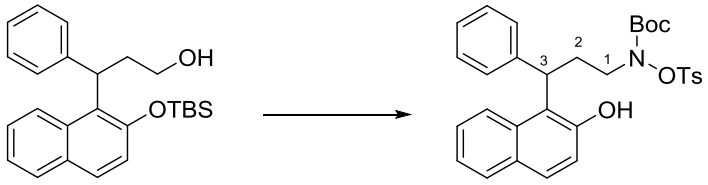
3-(2-((*tert*-Butyldimethylsilyl)oxy)naphthalen-1-yl)-3-phenylpropan-1-ol



This compound was prepared according to a literature procedure.[22]

ν_{max} / cm^{-1} (film) 3447 (m, br), 2952 (m), 2929 (m), 2857 (m), 1595 (m), 1463 (m), 1237 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 - 7.74 (1H, m), 7.76 - 7.68 (1H, m), 7.66 - 7.57 (1H, m), 7.32 - 7.24 (5H, m), 7.21 -7.15 (3H, m), 5.37 (1H, dd, *J* = 11.4, 4.7 Hz, C**3**-H), 3.62 - 3.53 (1H, m, C**1**-H), 3.37 - 3.27 (1H, m, C**1**-H'), 2.87 - 2.79 (1H, m, C**2**-H), 2.55 - 2.46 (1H, m, C**2**-H'), 2.28 (1H, br s, OH), 1.03 (9H, s, TBS (CH_3)$_3$), 0.37 (3H, s, TBS Si(CH_3)), 0.25 (3H, s, TBS Si(CH_3)); ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.6 (ArC), 144.6 (ArC), 132.8 (ArC), 130.8 (ArC), 128.5 (ArC), 128.8 (ArCH), 128.7 (ArCH), 128.3 (2 × ArCH), 127.1 (2 × ArCH), 125.7 (ArCH), 125.7 (ArCH), 125.5 (ArCH), 123.5 (ArCH), 120.2 (ArCH) 61.5 (C**1**), 36.4 (C**3**), 34.9 (C**2**) 25.9 (TBS (CH_3)$_3$), 18.4 (TBS SiC(CH_3)$_3$), -3.44 (TBS Si(CH_3)), -3.83 (TBS Si(CH_3)); HRMS (ESI$^+$) Calculated for $C_{25}H_{33}NaO_2Si$: 415.2064. Found $[M+Na]^+$: 415.2061.

***tert*-Butyl (3-(2-hydroxynaphthalen-1-yl)-3-phenylpropyl)(tosyloxy)carbamate (5p)**

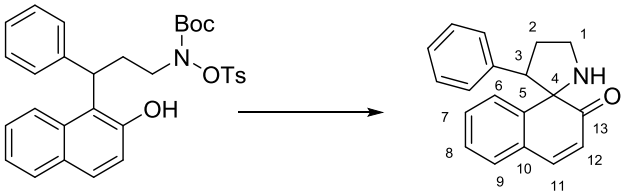


5p

General procedure C and D: 3-(2-((*tert*-Butyldimethylsilyl)oxy)naphthalen-1-yl)-3-phenylpropan-1-ol (0.27 g, 0.69 mmol), PPh_3 (0.22 g, 0.832 mmol), DIAD (0.16 mL, 0.83 mmol) and TsONHBoc (0.24 mg, 0.83 mmol) in anhydrous THF (4 mL) were employed. The product was purified by flash column chromatography (10 % EtOAc/hexane) to afford the desired product (0.40 g) which could not be obtained cleanly so was used crude in the next step using 1:1 TBAF/AcOH solution (0.1 M in THF, 0.60 mmol) in THF (12 mL). Purification by flash column chromatography (33 % EtOAc/hexane) afforded **5p** (0.26 g, 71% over 2 steps) as

an off-white solid; m.p.: 75 - 78 °C (EtOAc/hexane); R_f = 0.1 (20 % EtOAc/hexane); ν_{max} / cm^{-1} (film) 3410 (m, br), 2978 (m), 1721 (m), 1373 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 - 7.89 (1H, m, ArC<u>H</u>), 7.79 - 7.70 (3H, m, ArC<u>H</u>), 7.66 (1H, d, *J* = 8.8 Hz, ArC<u>H</u>), 7.46 - 7.37 (1H, m, ArC<u>H</u>), 7.35 - 7.26 (9H, m, ArC<u>H</u>), 7.00 (1H, d, *J* = 8.8 Hz, ArC<u>H</u>), 5.11 (1H, br s, O<u>H</u>), 4.99 (1H, t, *J* = 8.1 Hz, C**3**-<u>H</u>), 3.73 - 3.61 (1H, m, C**1**-<u>H</u>), 3.42-3.15 (1H,m, C**1**-<u>H</u>'), 2.84-2.51 (2H, m, C**2**-<u>H_2</u>), 2.37 (3H, s, Ts C<u>H_3</u>), 1.15 (9H, s, Boc (C<u>H_3</u>)$_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.6 (C=O), 151.9 (Ar<u>C</u>), 145.7 (Ts Ar<u>C</u>), 142.9 (Ar<u>C</u>), 133.2 (Ar<u>C</u>), 131.3 (Ts Ar<u>C</u>), 129.8 (Ar<u>C</u>), 129.7 (2 x Ts Ar<u>C</u>H), 129.6 (2 x Ts ArC<u>H</u>), 129.2 (ArC<u>H</u>), 129.0 (ArC<u>H</u>), 128.9 (Ar<u>C</u>H), 127.5 (Ar<u>C</u>H), 126.8 (Ar<u>C</u>H), 126.6 (Ar<u>C</u>H), 123.3 (Ar<u>C</u>H), 121.3 (Ar<u>C</u>), 119.2 (Ar<u>C</u>H), 83.6 (Boc <u>C</u>(CH_3)$_3$), 52.3 (C**1**), 38.4 (C**3**), 28.0 (C**2**), 27.7 (Boc (<u>C</u>H_3)$_3$), 21.8 (Ts <u>C</u>H_3)$_3$; HRMS (ESI^+) Calculated for $C_{31}H_{33}NNaO_6S$: 570.1920. Found $[M+Na]^+$: 570.1912.

3'-phenyl-2*H*-spiro[naphthalene-1,2'-pyrrolidin]-2-one (7p)



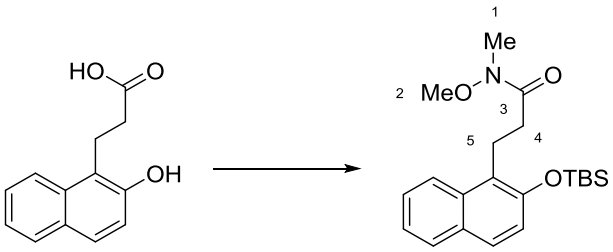
5p **7p**

General procedure E: *tert*-Butyl (3-(2-hydroxynaphthalen-1-yl)-3-phenylpropyl)(tosyloxy) carbamate (**5p**) (53.2 mg, 0.097 mmol) and TFA (15.0 μL, 0.19 mmol) in anhydrous TFE (1 mL) were employed. After stirring at r.t. for 22 h and purification by flash column chromatography (20% EtOAc/hexane) **7p** (19.2 mg, 72 %) was obtained as a 1:1 mixture of diastereomers A and B and as a pale-yellow solid. *The diastereomers could not be separated by column chromatography.*

Data for mixture of diastereomers A + B: R_f = 0.5 (50% EtOAc/hexane); ν_{max} / cm^{-1} (solid) 2961 (m), 2864 (m), 1650 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (1H, d, *J* = 7.8 Hz, C**6**-<u>H</u>, *B*), 7.68 (1H, d, *J* = 7.8 Hz, C**6**-<u>H</u>, *A*), 7.47 (1H, td, *J* = 7.6, 1.4 Hz, C**7**-<u>H</u>, *B*), 7.38 (1H, td, *J* = 7.6, 1.3 Hz, C**7**-<u>H</u>, *A*), 7.30 - 7.25 (1H, m, C**8**-<u>H</u>, *B*), 7.18 - 7.09 (5H, m, 3 × PhC<u>H</u>, *B*, C**8**-<u>H</u>, *A*, C**9**-<u>H</u>, *B*), 7.05 - 7.00 (1H, m, PhC<u>H</u>, *A*), 6.93 - 6.90 (2H, m, 2 × PhC<u>H</u>, *A*), 6.85 - 6.81 (2H, m, C**9**-<u>H</u>, *A*, C**11**-<u>H</u>, *A*), 6.77 (1H, d, *J* = 9.9 Hz, C**11**-<u>H</u>, *B*), 6.71 - 6.68 (2H, m, 2 × Ph<u>C</u>H, *B*), 6.52 - 6.48 (2H, m, 2 × Ph<u>C</u>H, *A*), 6.03 (1H, d, *J* = 9.8 Hz, C**12**-<u>H</u>, *A*), 5.44 (1H, d, *J* = 9.9 Hz, C**12**-<u>H</u>, *B*), 3.69 (1H, ddd, *J* = 10.7, 8.1 Hz, C**1**-<u>H</u>, *B*), 3.56 - 3.49 (2H, m, C**1**-<u>H_2</u>, *A*), 3.40 -

3.25 (3H, m, C**3**-H, *A*+*B*, C**1**-H', *B*), 2.69 (2H, br s, NH, *A*+B), 2.57 - 2.46 (1H, m, C**2**-H, *B*), 2.44 - 2.33 (1H, m, C**2**-H, *A*), 2.22 - 1.26 (1H, m, C**2**-H', *A*), 2.04 - 1.98 (1H, m, C**2**-H', *B*); ^{13}C NMR (101 MHz, $CDCl_3$) δ 205.8 (C**13**, *B*), 205.2 (C**13**, *A*), 147.7 (C**5**, *B*) , 145.9 (C**11**, *A*), 145.0 (C**5**, *A*), 143.8 (C**11**, *B*), 137.1 (PhC, *B*), 136.9 (PhC, *A*), 130.9 (C**10**, *A*), 130.5 (C**10**, *B*), 130.5 (C**7**, *B*), 129.3 (C**7**, *A*), 129.2 (2 × PhCH *A*), 128.7 (C**9**, *A*), 128.6 (PhCH, *B*), 128.1 (PhCH, *B*), 128.0 (C**6**, *A*), 127.6 (2 × PhCH, *B*), 127.3 (C**8,** *B*), 127.4 (C**8**, *A*/ C**9**, *B*), 127.3 (C**8**, *A*/ C**9**, *B*), 127.0 (PhCH, *A*), 126.9 (2 × PhCH, *A*), 126.8 (C**6**, *B*), 124.9 (C**12**, *B*), 124.1 (C**12**, *A*), 78.1 (C**4**, *A*), 77.2 (C**4**, *B*), 64.5 (C**3**, *A*/*B*), 61.8 (C**3**, *A*/*B*), 48.3 (C**1**, *B*), 47.3 (C**1**, *A*), 32.0 (C**2**, *A*), 30.0 (C**2**, *B*); HRMS (ESI$^+$) Calculated for $C_{19}H_{17}NNaO$: 298.1202. Found $[M+Na]^+$: 298.1200.

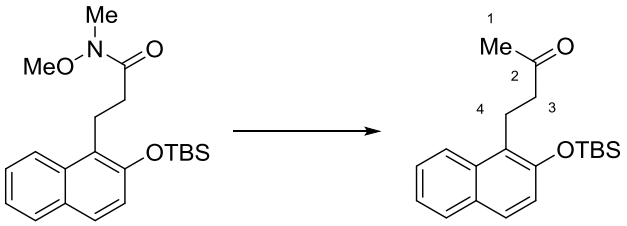
3-(2-((*tert*-Butyldimethylsilyl)oxy)naphthalen-1-yl)-*N*-methoxy-*N*-methylpropanamide



General procedure H: 3-(2-((*tert*-Butyldimethylsilyl)oxy)naphthalen-1-yl)propanoic acid (2.64 g, 8.00 mmol), *N*,*O*-dimethylhydroxylamine hydrochloride (1.09 g, 11.2 mmol), Et_3N (1.56 mL, 11.2 mmol), 4-dimethylaminopyridine (1.37 g, 11.2 mmol), and *N*,*N*'-dicyclohexylcarbodiimide (2.31 g, 11.2 mmol) were employed. Purification by flash column chromatography (20 % EtOAc/hexane) afforded 3-(2-((*tert*-butyldimethylsilyl)oxy) naphthalen-1-yl)-*N*-methoxy-*N*-methylpropanamide (2.20 g, 74 %) as a pale yellow oil; R_f = 0.7 (33 % EtOAc/hexane); ν_{max} / cm^{-1} 2954 (m), 2930 (m), 2857 (m), 1664 (s), 1594 (m), 1466 (s), 1379 (m), 1242 (s), 1072 (m); ^{1}H NMR (400 MHz, $CDCl_3$) 8.02 (1H, d, *J* = 8.5 Hz, ArCH) δ 7.78 (1H, d, *J* = 8.4 Hz, ArCH), 7.64 (1H, d, *J* = 8.9 Hz, ArCH), 7.51 - 7.47 (1H, m, ArCH), 7.37 - 7.32 (1H, m, ArCH), 7.11 (1H, d, *J* = 8.8 Hz, ArCH), 3.59 (3H, s, C**2**-H_3), 3.41 (2H, t, *J* = 8.1 Hz, C**5**-H_2), 3.21 (3H, s, C**1**-H_3), 2.73 (2H, t, *J* = 8.1 Hz, C**4**-H_2), 1.07 (9H, s, TBS (CH_3)$_3$), 0.30 (6H, s, TBS Si(CH_3)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.2 (C**3**) 150.7 (ArC), 133.2 (ArC), 129.5 (ArC), 128.5 (ArCH), 127.5 (ArCH), 126.3 (ArCH), 124.3 (ArC), 123.3 (ArCH), 123.1 (ArCH), 120.3 (ArCH), 61.2 (C**2**), 32.3 (C**4**), 31.9 (C**1**), 25.8 (TBS (CH_3)$_3$),

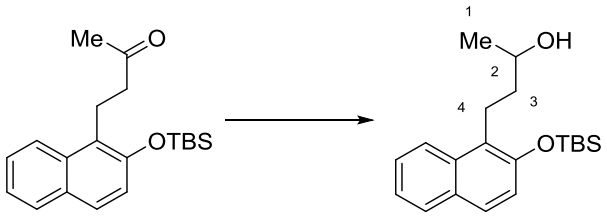
20.7 (C**5**), 18.3 (TBS $\underline{C}(CH_3)_3$), -3.9 (TBS Si($\underline{C}H_3)_2$); HRMS (ESI^+) Calculated for $C_{21}H_{31}NNaO_3Si$: 396.1965. Found $[M+Na]^+$: 396.1976.

4-(2-((*tert*-Butyldimethylsilyl)oxy)naphthalen-1-yl)butan-2-one



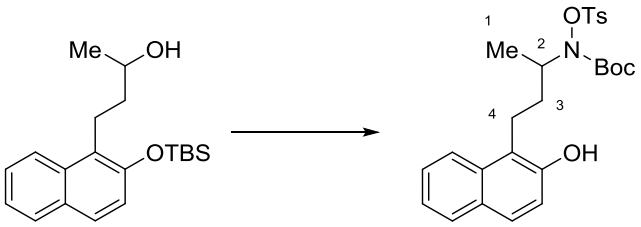
To a solution of 3-(2-((*tert*-butyldimethylsilyl)oxy)naphthalen-1-yl)-*N*-methoxy-*N*-methyl propanamide (0.94 g, 2.50 mmol) in anhydrous THF (6 mL) at 0 ^{o} C was added methylmagnesium bromide (3 M in Et_2O, 1.6 mL, 5.0 mmol) dropwise over 5 min. The reaction mixture was stirred at r.t. for 1 h until completion by TLC analysis. The reaction mixture was quenched by addition of sat. aq. NH_4Cl (5 mL) and the aqueous phase was extracted with EtOAc (3 × 5mL). The combined organic extracts were washed with brine (10 mL), dried over Na_2SO_4 and concentrated *in vacuo* to afford the title compound (0.61 g, 74 %) as a pale yellow oil which was used without further purification; R_f = 0.8 (33 % EtOAc/hexane); ν_{max} / cm^{-1} 2954 (m), 2929 (m), 2893 (m), 2857 (m), 1713 (s), 1622 (m), 1594 (m), 1466 (s), 1360 (m), 1242 (s), 1161 (m), 1075 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (1H, d, *J* = 8.5 Hz, ArC$\underline{H}$), 7.79 (1H, d, *J* = 8.4 Hz, ArC$\underline{H}$), 7.64 (1H, d, *J* = 8.8 Hz, ArC$\underline{H}$), 7.49 (1H, ddd, *J* = 8.4, 6.8, 1.4 Hz, ArC$\underline{H}$), 7.35 (1H, ddd, *J* = 8.0, 6.8, 1.1 Hz, ArC$\underline{H}$), 7.10 (1H, d, *J* = 8.8 Hz, ArC$\underline{H}$), 3.33 (2H, t, *J* = 8.2 Hz, C**4**-$\underline{H}_2$), 2.74 (2H, t, *J* = 8.2 Hz, C**3**-$\underline{H}_2$), 2.18 (3H, s, C**1**-$\underline{H}_3$), 1.06 (9H, s, TBS ($C\underline{H}_3)_3$), 0.29 (6H, s, TBS Si($C\underline{H}_3)_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 208.5 (C**2**), 150.6 (Ar$\underline{C}$), 133.0 (Ar$\underline{C}$), 129.5 (Ar$\underline{C}$), 128.6 (Ar$\underline{C}$H), 127.5 (Ar$\underline{C}$H), 126.4 (Ar$\underline{C}$H), 123.9 (Ar$\underline{C}$), 123.4 (Ar$\underline{C}$H), 122.9 (Ar$\underline{C}$H), 120.2 (Ar$\underline{C}$H), 43.5 (C**3**), 29.9 (C**1**), 25.8 (TBS ($\underline{C}H_3)_3$), 19.9 (C**4**), 18.3 (TBS $\underline{C}(CH_3)_3$), -3.9 (TBS Si($\underline{C}H_3)_2$); HRMS (ESI^+) Calculated for $C_{20}H_{28}NaO_2Si$: 351.1750. Found $[M+Na]^+$: 351.1753.

4-(2-((*tert*-Butyldimethylsilyl)oxy)naphthalen-1-yl)butan-2-ol



To a solution of 4-(2-((*tert*-butyldimethylsilyl)oxy)naphthalen-1-yl)butan-2-one (0.56 g, 1.70 mmol) in MeOH (10 mL) was slowly added $NaBH_4$ (0.13 mg, 3.40 mmol) at 0 °C. The reaction was stirred at this temperature for 1.5 h until complete by TLC analysis. The reaction was quenched by addition of water (10 mL) and extracted with Et_2O (3 × 10 mL). The combined organic extracts were washed with brine (10 mL), dried over $MgSO_4$, filtered and the solvent removed *in vacuo* to afford the title compound (0.49 g, 87 %) as a pale yellow oil which was used without further purification.; R_f = 0.6 (33 % EtOAc/hexane); ν_{max} / cm^{-1} 3360 (m br), 2957 (m), 2928 (m), 2884 (m), 2857 (m), 1622 (m), 1594 (m), 1465 (m), 1241 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (1H, d, *J* = 8.4 Hz), 7.78 (2H, d, *J* = 8.3 Hz), 7.62 (1H, d, *J* = 8.8 Hz), 7.48 (1H, ddd, *J* = 8.4, 6.8, 1.4 Hz), 7.35 (1H, ddd, *J* = 8.0, 6.8, 1.1 Hz), 7.10 (1H, d, *J* = 8.9 Hz), 3.73-3.65 (1H, m, C**2**-H), 3.27-3.13 (2H, m, C**4**-H_2), 2.29 (1H, br s, OH), 1.87 - 1.74 (2H, m, C**3**-H_2), 1.19 (3H, d, *J* = 6.2 Hz, C**1**-H_3), 1.06 (9H, s, TBS (CH_3)$_3$), 0.29 (6H, s, TBS Si(CH_3)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.3 (Ar**C**), 133.2 (Ar**C**), 129.8 (Ar**C**), 128.5 (Ar**C**H), 127.3 (Ar**C**H), 126.2 (Ar**C**H), 124.8 (Ar**C**H), 123.5 (Ar**C**), 123.4 (Ar**C**H), 120.5 (Ar**C**H), 67.1 (C**2**), 38.9 (C**3**), 25.9 (TBS (**C**H_3)$_3$), 23.1 (C**4**), 21.6 (C**1**), 18.4 (TBS Si**C**(CH_3)$_3$), -3.9 (TBS Si(**C**H_3)$_2$); HRMS (ESI$^+$) Calculated for $C_{20}H_{30}NaO_2Si$: 353.1907. Found $[M+Na]^+$: 353.1894.

***tert*-Butyl (4-(2-hydroxynaphthalen-1-yl)butan-2-yl)(tosyloxy)carbamate (5q)**

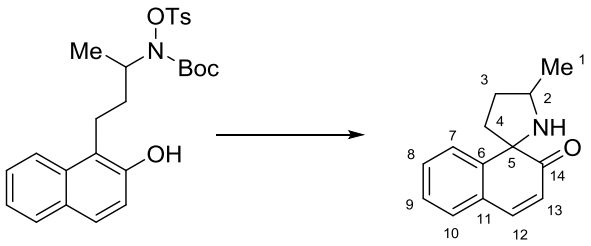


5q

General procedure C and D: 4-(2-((*tert*-Butyldimethylsilyl)oxy)naphthalen-1-yl)butan-2-ol (0.22 g, 0.77 mmol), PPh_3 (0.24 g, 0.92 mmol), DIAD (0.18 mL, 0.92 mmol) and TsONHBoc (0.26 g, 0.92 mmol) in anhydrous THF (3 mL) were employed. The desired product could not be obtained pure so to the crude product in THF (5 mL) was added a solution of TBAF (1M in THF, 1.06 mL, 1.06 mmol) at 0 °C. The reaction mixture was stirred at this temperature for 1.5 h until complete by TLC. The reaction mixture was quenched with sat. aq. NH_4Cl (5 mL) and extracted with EtOAc (3 × 5 mL). The combined organic extracts were washed with brine (10 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by flash column

chromatography (gradient 20 – 33 % EtOAc/hexane) afforded **5q** (0.32 g, 69 %) as a colorless solid; R_f = 0.4 (33 % EtOAc/hexane); ν_{max} / cm^{-1} (solid) 3461 (m, br) 2975 (m), 1688 (s), 1386 (s); ^{1}H NMR (400 MHz, CD_3OD) δ 7.83 (3H, d, *J* = 8.3, Ts ArC<u>H</u>, ArC<u>H</u>), 7.72 (1H, d, *J* = 8.1 Hz, ArC<u>H</u>), 7.58 (1H, d, *J* = 8.8 Hz, ArC<u>H</u>), 7.42 - 7.33 (3H, m, ArC<u>H</u>), 7.24 (1H, t, *J* = 7.5 Hz, ArC<u>H</u>), 7.09 (1H, d, *J* = 8.8 Hz, ArC<u>H</u>), 4.00 (1H, sextet, *J* = 6.9 Hz, C**2**-<u>H</u>), 3.03 (2H, dd, *J* = 9.3, 6.6 Hz, C**4**-<u>H_2</u>), 2.38 (3H, s, Ts C<u>H_3</u>), 1.94 - 1.83 (1H, m, C**3**-<u>H</u>), 1.77 - 1.66 (1H, m, C**3**-<u>H</u>'), 1.27 (3H, d, *J* = 6.7 Hz, C**1**-<u>H_3</u>), 1.20 (9H, s, Boc (C<u>H_3</u>)$_3$); ^{13}C NMR (101 MHz, CD_3OD) δ 157.9 (C=O), 153.3 (Ar<u>C</u>), 147.4 (Ts Ar<u>C</u>), 134.7 (Ar<u>C</u>), 132.9 (Ar<u>C</u>), 130.8 (2 × Ts Ar<u>C</u>H), 130.7 (2 × Ts Ar<u>C</u>H), 130.4 (Ar<u>C</u>), 129.5 (Ar<u>C</u>H), 128.5 (Ar<u>C</u>H), 127.1 (Ar<u>C</u>H), 123.7 (Ar<u>C</u>H), 123.4 (Ar<u>C</u>H), 120.3 (Ar<u>C</u>), 118.6 (Ar<u>C</u>H), 84.7 (Boc <u>C</u>(CH$_3$)$_3$, 62.8 (C**2**), 35.2 (C**3**), 27.9 (Boc (<u>C</u>H_3)$_3$), 22.8 (C**4**), 21.6 (Ts <u>C</u>H_3), 17.8 (C**1**); HRMS (ESI$^+$) Calculated for $C_{26}H_{31}NNaO_6Si$: 508.1764. Found [M+Na]$^+$: 508.1756.

5'-Methyl-2*H*-spiro[naphthalene-1,2'-pyrrolidin]-2-one (7q)



5q **7q**

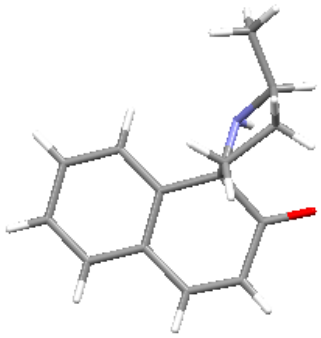
General procedure E: *tert*-Butyl (4-(4-hydroxyphenyl)butan-2-yl)(tosyloxy)carbamate (**5q**) (97.1 mg, 0.20 mmol) and TFA (30 μL, 0.4 mmol) in 5:1 TFE/CH_2Cl_2 (3 mL) were stirred at r.t. for 48 h. Purification by flash column chromatography (20 – 33 % EtOAc/hexane – 100 % EtOAc) afforded **7q** (23.0 mg, 54 %) as a 1.5:1 mixture of diastereomers A and B and as a yellow solid.

R_f = 0.5 (2:1 EtOAc/hexane); ν_{max} / cm^{-1} 3337 (s), 2963 (s), 2916 (s), 2850 (s), 1668 (s), 1084 (s); HRMS (ESI$^+$) Calculated for $C_{14}H_{15}NNaO$: 236.1046. Found [M+Na]$^+$: 236.1046.

Data for the major diastereomer: m.p.: 89 - 90 °C (EtOAc/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (1H, d, *J* = 7.8 Hz, C**7**-<u>H</u>), 7.41 - 7.35 (2H, m, C**8**-<u>H</u>, C**12**-<u>H</u>), 7.26 - 7.24 (2H, m, C**9**-<u>H</u>, C**10**-<u>H</u>), 6.18 (1H, d, *J* = 9.9 Hz, C**13**-<u>H</u>), 3.63 - 3.55 (1H, m, C**2**-<u>H</u>), 2.42 (1H , br s, N<u>H</u>) overlapping 2.45 - 2.39 (1H, ddd, *J* = 12.9, 7.0, 2.8 Hz, C**4**-<u>H</u>), 1.92 - 1.86 (1H, dddd, *J* = 11.5, 6.4, 5.1, 2.8 Hz, C**3**-<u>H</u>), 1.82 - 1.74 (1H, ddd, *J* = 13.0, 10.8, 6.2 Hz, C**4**-<u>H</u>'), 1.42 - 1.35 (1H,

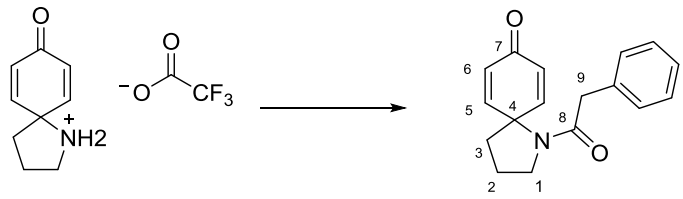
m, C**3**-H') overlapping 1.39 (3H, d, *J* = 6.2 Hz, C**1**-H$_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 204.3 (C**14**), 149.1 (C**6**), 144.6 (C**12**), 130.4 (C**8**), 129.1 (C**10**), 128.9 (C**11**), 126.9 (C**9**), 125.8 (C**7**), 123.4 (C**13**), 74.8 (C**5**), 58.2 (C**2**), 42.9 (C**4**), 33.3 (C**3**), 20.2 (C**1**).

Data for the minor diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (1H, dd, *J* = 7.8, 1.0 Hz), 7.42 - 7.32 (2H, m, C**8**-H, C**12**-H), 7.28 - 7.22 (2H, m, C**9**-H, C**10**-H), 6.15 (1H, d, *J* = 9.9 Hz, C**13**-H), 3.76 - 3.67 (1H, m, C**2**-H), 2.72 (1H, br s, NH), 2.25 (1H, ddd, *J* = 12.4, 10.1, 6.8 Hz, C**4**-H), 1.90 (1H, dddd, *J* = 12.4, 6.8, 5.7, 3.5 Hz, C**3**-H), 1.81 (1H, ddd, *J* = 12.4, 6.8, 3.5 Hz, C**4**-H'), 1.53 (1H, dddd, *J* = 11.8, 10.0, 8.9, 6.9 Hz, C**3**-H'), 1.33 (3H, d, *J* = 6.2 Hz, C**1**-H$_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.5 (C**14**), 149.2 (C**6**), 144.4 (C**12**) 130.0 (C**8**), 129.5 (C**10**), 129.2 (C**11**), 127.1 (C**9**), 126.6 (C**7**), 124.0 (C**13**), 74.0 (C**5**), 55.9 (C**2**), 42.7 (C**4**), 32.6 (C**3**), 22.3 (C**1**).



The stereochemistry of the major diastereomer was determined unambiguously by X-ray crystallography.

1-(2-Phenylacetyl)-1-azaspiro[4.5]deca-6,9-dien-8-one (9a)

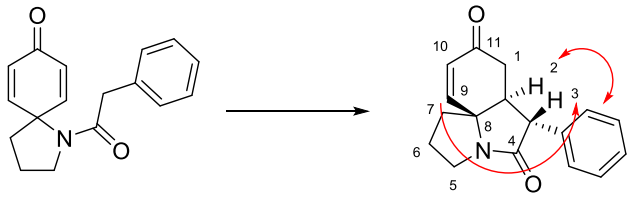


7a **9a**

A solution of 1-Azaspiro[4.5]deca-6,9-dien-8-one trifluoroacetate (**7a**) (19.2 mg, 0.073 mmol) in anhydrous THF (0.36 mL) under an atmosphere of nitrogen was cooled to 0 °C and phenylacetyl chloride (19.4 μL, 0.147 mmol) and K_3PO_4 (62.2 mg, 0.293 mmol) were added.

The reaction was warmed to r.t. and stirred overnight and monitored by TLC. Upon completion, the reaction was quenched with water (1 mL) and extracted with EtOAc (3 x 2 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated *in vacuo*. Purification by flash column chromatography (gradient, eluent 50 % EtOAc/pentane – 100 % EtOAc) afforded **9a** (12.2 mg, 63 %) as a 3:1 mixture of rotamers *A*+*B* and as a colorless, viscous oil; R_f = 0.3 (3% MeOH/CH_2Cl_2); ν_{max} / cm^{-1} (film) 3029 (m), 2972 (m), 2881 (m), 1659 (s), 1622 (s), 1395 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 - 7.10 (5H, m, 5 × PhC<u>H</u>, *A* + *B*), 6.95 (0.50 H, d, *J* = 10.0 Hz, 0.50 × C**5**-<u>H</u>, *B*), 6.76 (1.50 H, d, *J* = 10.0 Hz, 1.50 × C**5**-<u>H</u>, *A*), 6.32 (0.50 H, d, *J* = 10.0 Hz, 0.50 H × C**6**-<u>H</u>, *B*), 6.25 (1.50 H, d, *J* = 10.0 Hz, 1.5 × C**6**-<u>H</u>, *A*), 3.86 (0.5 H, t, *J* = 6.9 Hz, 0.50 × C**1**-<u>H_2</u>, *B*), 3.71 (1.50 H, t, *J* = 6.9 Hz, 1.50 × C**1**-<u>H_2</u>, *A*), 3.65 (1.50 H, s, 1.50 × C**9**-<u>H_2</u>, *A*), 3.43 (0.50 H, s, 0.50 × C**9**-<u>H_2</u>, *B*), 2.25 (0.50 H, t, *J* = 6.9 Hz, 0.50 × C**3**-<u>H_2</u>, *B*), 2.12 - 1.99 (3.5 H, m, 3.5 H x C**2** + C**3**-<u>H_2</u>, *A* + *B*); ^{13}C NMR (101 MHz, $CDCl_3$) δ 185.4 (C**7**, *A*), 184.4 (C**7**, *B*), 170.7 (C**8**, *B*), 169.5 (C**8**, *A*), 51.2 (C**5**, *B*) 150.7 (C**5**, *A*), 134.8 (Ph<u>C</u>, *B*), 134.2 (Ph<u>C</u>, *A*), 129.4 (Ph<u>C</u>H, *B*), 129.0 (2 × Ph<u>C</u>H, *A*), 128.9 (2 × Ph<u>C</u>H, *A*), 128.7 (Ph<u>C</u>H, *B*), 128.5 (C**6**, *B*), 128.3 (C**6**, *A*), 127.1 (Ph<u>C</u>H, *A*), 126.9 (Ph<u>C</u>H, *B*), 62.7 (C**4**, *A*), 62.0 (C**4**, *B*), 49.0 (C**1**, *B*), 48.5 (C**1**, *A*), 42.8 (C**9**, *A*), 42.0 (C**3**, *B*), 39.9 (C**9**, *B*), 38.9 (C**3**, *A*), 24.5 (C**2**, *A*), 22.6 (C**2**, *B*); HRMS (ESI^+) Calculated for $C_{17}H_{18}NO_2$: 268.1332. Found $[M+H]^+$: 268.1325.

(6*R, 6a*S**, 10a*S**)-6-Phenyl-2,3,6a,7-tetrahydro-1*H*,5*H*-pyrrolo[2,1-i]indole-5,8(6*H*)-dione (10a)**



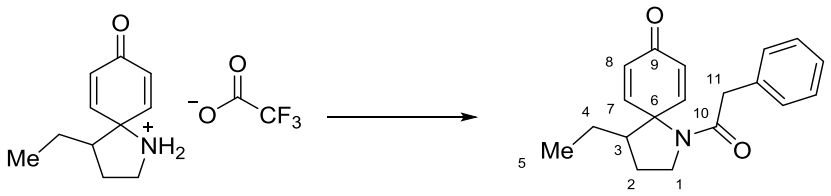
9a **10a**

To a solution of 1-(2-phenylacetyl)-1-azaspiro[4.5]deca-6,9-dien-8-one (**9a**) (26.7 mg, 0.10 mmol) in anhydrous THF (1 mL) at -78 °C and under an atmosphere of nitrogen was added 1.5 eq. lithium bis(trimethylsilyl)amide (1.0 M in THF, 0.15 mL, 0.15 mmol). The reaction was stirred at this temperature for 2 h and monitored by TLC. Upon completion, the reaction mixture was warmed to 0 °C and quenched with sat. aq. NH_4Cl (0.3 mL) and extracted with EtOAc (3 × 5 mL). The combined organic extracts were washed with brine (5 mL), dried over

anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. Purification by flash column chromatography (EtOAc) afforded **10a** (17.9 mg, 67 %, > 20:1 d.r.) as a colorless oil; R_f = 0.4 (3 % MeOH/CH_2Cl_2); ν_{max} / cm^{-1} (film) 2920 (m), 1677 (br s), 1395 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 - 7.27 (3H, m, PhC<u>H</u>), 7.15 - 7.11 (2H, m, PhC<u>H</u>), 6.64 (1H, dd, *J* = 10.3, 1.9 Hz, C**9**-<u>H</u>), 6.13 (1H, dd, *J* = 10.3, 1.1 Hz, C**10**-<u>H</u>), 3.97 (1H, ddd, *J* = 12.4, 7.3, 5.2 Hz, C**5**-<u>H</u>), 3.68 (1H, d, *J* =12.2 Hz, C**3**-<u>H</u>), 3.28 - 3.20 (1H, m, C**5**-<u>H</u>'), 2.71 - 2.62 (2H, m, C**2**-<u>H</u>, C**1**-<u>H</u>), 2.49 - 2.43 (1H, m, C**1**-<u>H</u>'), 2.32 - 2.21 (1H, m, C**6**-<u>H</u>), 2.19 - 2.11 (1H, m, C**6**-<u>H</u>'), 2.10 - 2.02 (2H, m, C**7**-<u>H_2</u>); ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.0 (C**11**), 173.5 (C**4**), 146.9 (C**9**), 135.7 (Ph<u>C</u>), 129.2 (2 × Ph<u>C</u>H), 129.0 (2 × Ph<u>C</u>H), 128.0 (C**10**), 127.8 (Ph<u>C</u>H), 65.3 (C**8**), 56.3 (C**3**), 51.5 (C**2**), 42.7 (C**5**), 36.3 (C**1**), 35.6 (C**7**), 26.3 (C**6**). HRMS (ESI^+) Calculated for $C_{17}H_{17}NNaO_2$: 290.1151. Found $[M+Na]^+$: 290.1155.

*The relative stereochemistry of this compound was determined by nOe experiments as indicated on the compound structure. nOes were observed between C**3**-<u>H</u> and C**9**-<u>H</u>.*

4-Ethyl-1-(2-phenylacetyl)-1-azaspiro[4.5]deca-6,9-dien-8-one (9g)

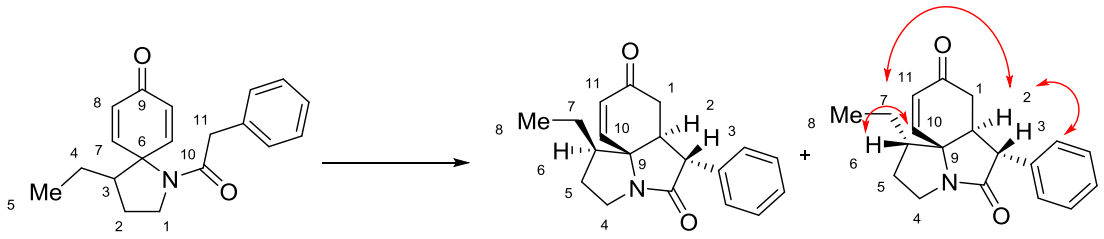


7g **9g**

The title compound was prepared using the same procedure as for **9a** using 4-Ethyl-1-azaspiro[4.5]deca-6,9-dien-8-one salt (**7g**) (43.7 mg, 0.15 mmol), 2.5 eq. phenylacetyl chloride (26 μL, 0.2 mmol) and K_3PO_4 (67.9 mg, 0.32 mmol) in anhydrous THF (1 mL). Purification by flash column chromatography (gradient, eluent 50% EtOAc/pentane – 100% EtOAc) afforded **9g** (18.7 mg, 79 %) as a 2.3:1 mixture of rotamers *A*:*B* and a colorless oil; R_f = 0.3 (3 % MeOH/CH_2Cl_2); ν_{max} / cm^{-1} (film) 2962 (m), 2930 (m), 2876 (m), 1660 (s), 1623 (s), 1454 (m), 1397 (s), 1384 (s), 719 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 - 7.17 (4.40 H, m, PhC<u>H</u>, *A*+*B*), 7.13 - 7.10 (0.60 H, m, 2 × Ph<u>C</u>H, *B*), 6.82 - 6.70 (0.60 H, m, 0.60 × C**7**-<u>H</u>, *B*), 6.67 (0.70 H, dd, *J* = 10.0, 3.0 Hz, 0.70 × C**7**-<u>H</u>, *A*), 6.57 (0.70 H, dd, *J* = 10.0, 3.0 Hz, 0.70 × C**7**-<u>H</u>, *A*), 6.40 - 6.34 (0.60 H, m, 0.60 × C**8**-<u>H</u>, *B*), 6.34 - 6.26 (1.40 H, m, 1.40 × C**8**-<u>H</u>, *A*), 4.09 (0.3 H, dd, *J* = 12.3, 8.1 Hz, 0.3 × C**1**-<u>H</u>), 3.82 (0.7 H, t, *J* = 9.2 Hz, 0.7 × C**1**-<u>H</u>), 3.65 - 3.52

(2.40 H, m, 2.40 × C**1**-H', *A*+*B*, C**11**-H$_2$, *A*), 3.43 (0.6 H, d, *J* = 4.6 Hz, 0.6 × C**11**-H$_2$, *B*), 2.31 - 2.25 (1H, m, C**2**-H, *A*+*B*), 2.23 - 2.14 (0.30 H, m, 0.30 × C**3**-H, *B*), 2.02 - 1.95 (0.70 H, m, 0.70 × C**3**-H, *A*), 1.76 - 1.64 (0.70 H, m, 0.70 × C**2**-H', *A*), 1.63 - 1.55 (0.3 H, m, 0.30 × C**2**-H', *B*), 1.27 - 1.17 (1H, m, C**4**-H, *A*+*B*), 1.06 - 0.95 (1H, m, C**4**-H', *A*+*B*), 0.93 - 0.84 (3H, m, C**5**-H$_3$, *A*+*B*); ^{13}C NMR (101 MHz, $CDCl_3$) δ 185.8 (C**9**, *A*), 184.7 (C**9**, *B*), 170.6 (C**10**, *B*), 169.5 (C**10**, *A*), 152.1 (C**7**, *A*), 152.0 (C**7**, *B*), 147.8 (C**7**, *B*), 146.4 (C**7**, *A*), 134.8 (PhC, *B*), 134.1 (PhC, *A*), 130.4 (C**8**, *A*), 129.9 (C**8**, *B*), 129.6 (C**8**, *B*), 129.3 (PhCH, *B*), 128.9 (PhCH, *A* + *B*), 128.7 (PhCH, *A* + *B*), 128.3 (PhCH, *A* + *B*), 128.2 (C**8**, *A*), 126.9 (PhCH, *A* + *B*), 126.7 (PhCH, *B*), 65.7 (C**6**, *A*), 65.5 (C**6**, *B*), 53.5 (C**3**, *B*), 50.6 (C**3**, *A*), 47.4 (C**1**, *B*), 47.3 (C**1**, *A*), 42.5 (C**11**, *A*), 40.1 (C**11**, *B*), 29.9 (C**2**, *A*), 27.8 (C**2**, *B*), 21.3 (C**4**, *A* + *B*), 12.5 (C**5**, *A* + *B*); HRMS (ESI$^+$) Calculated for $C_{19}H_{21}NNaO_2$: 318.1464. Found $[M+Na]^+$: 318.1472.

(1*R, 6*R**, 6a*S**, 10a*S**) *and* (1*S**, 6*R**, 6a*S**, 10a*S**)-1-Ethyl-6-phenyl-2,3,6a,7-tetrahydro-1*H*,5*H*-pyrrolo[2,1-i]indole-5,8(6*H*)-dione (10g)**



9g **10g**

The title compound was prepared using the same procedure as for **10a** employing 4-ethyl-1-(2-phenylacetyl)-1-azaspiro[4.5]deca-6,9-dien-8-one (**9g**) (29.5 mg, 0.100 mmol) and 1.5 eq. lithium bis(trimethylsilyl)amide (1 M in THF) in anhydrous THF (1 mL). Purification by flash column chromatography (50 % EtOAc/hexane) afforded **10g** (16.6 mg, 56 %) as a 3:1 mixture of diastereomers A and B and as a colorless solid.

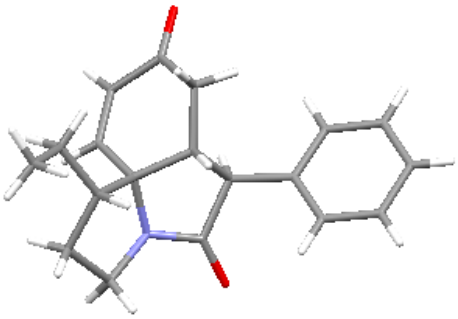
R_f = 0.6 (3% MeOH/CH_2Cl_2); ν_{max} / cm^{-1} (solid) 2963 (m), 2929 (m), 2877 (m), 1693 (s), 1675 (s), 1394 (s); HRMS (ESI$^+$) Calculated for $C_{19}H_{21}NNaO_2$: 318.1464. Found $[M+Na]^+$: 318.1469.

Data for the major diastereomer A: m.p. 194 °C (EtOAc/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 - 7.32 (2H, m, PhCH), 7.30 - 7.24 (1H, m, PhCH), 7.15 - 7.12 (2H, m, PhCH), 6.62 (1H,

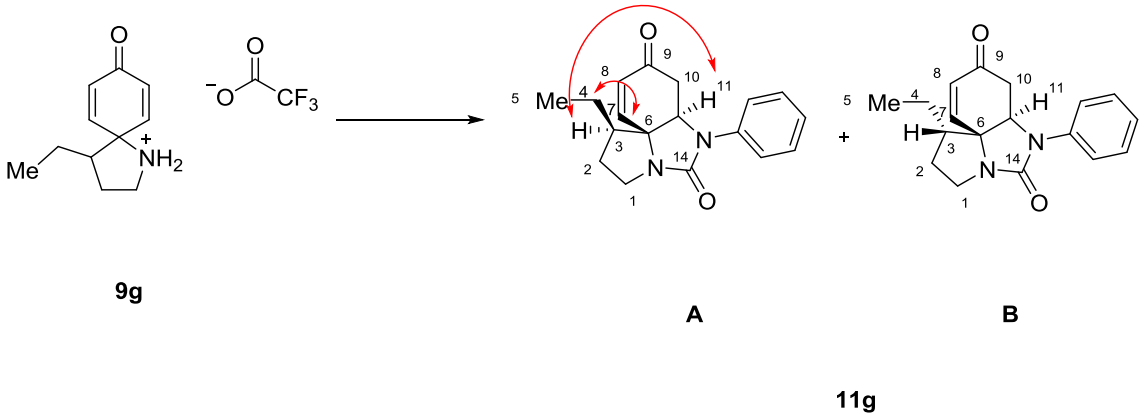
dd, *J* = 10.4, 1.7 Hz, C**10**-H), 6.22 (1H, d, *J* = 10.4 Hz, C**11**-H), 3.77 - 3.71 (1H, m, C**4**-H), 3.68 (1H, d, *J* = 12.0 Hz, C**3**-H), 3.43 (1H, t, *J* = 10.6 Hz, C**4**-H'), 2.71 (1H, dd, *J* = 12.3, 6.1 Hz, C**2**-H), 2.65 - 2.53 (2H, m, C**1**-H, C**5**-H), 2.50 - 2.43 (1H, m, C**1**-H'), 2.10 - 1.91 (2H, m, C**6**-H, C**5**-H'), 1.62 - 1.52 (1H, m, C**7**-H), 1.37 - 1.23 (1H, m, C**7**-H'), 0.99 (3H, t, *J* = 7.4 Hz, C**8**-H_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.3 (C=O) , 171.8 (C=O), 144.1 (C**10**), 135.8 (PhC), 129.8 (C**11**), 129.3 (2 × PhCH), 128.9 (2 × PhCH), 127.8 (PhCH), 67.7 (C**9**), 57.8 (C**3**), 51.7 (C**2**), 51.4 (C**6**), 40.5 (C**4**), 36.8 (C**1**), 32.3 (C**5**), 23.7 (C**7**), 13.0 (C**8**).

Data for the minor diastereomer B: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 - 7.32 (2H, m, PhCH), 7.32 - 7.28 (1H, m, PhCH), 7.14 - 7.10 (2H, m, PhCH), 6.58 (1H, dd, *J* = 10.2, 1.9 Hz, C**10**-H), 6.16 (1H, dd, *J* = 10.2, 0.9 Hz, C**11**-H), 4.05 (1H, ddd, *J* = 10.8, 7.3, 2.7 Hz, C**4**-H), 3.62 (1H, d, *J* = 12.3 Hz, C**3**-H), 3.14 - 3.06 (1H, m, C**4**-H'), 2.76 (1H, dd, *J* = 12.4, 5.7 Hz, C**2**-H), 2.56 - 2.41 (2H, m, C**1**-H_2), 2.33 - 2.25 (1H, m, C**5**-H), 2.17 - 2.08 (1H, m, C**6**-H), 1.78 - 1.68 (1H, m, C**7**-H), 1.64 - 1.55 (1H, m, C**5**-H'), 1.47 - 1.35 (1H, m, C**7**-H'), 1.03 (3H, t, *J* =7.3 Hz, C**8**-H_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.1 (C=O), 174.6 (C=O), 148.8 (C**10**), 135.8 (PhC), 129.4 (2 × PhCH), 129.0 (2 × PhCH), 128.2 (C**11**), 127.9 (PhCH), 66.4 (C**9**), 55.6 (C**3**), 48.9 (C**6**), 46.3 (C**2**), 42.9 (C**4**), 36.2 (C**1**), 31.9 (C**5**), 22.4 (C**7**), 13.2 (C**8**).

*The relative stereochemistry of the minor diastereomer was determined by nOe experiments as indicated on the compound structure; nOes were observed between C**2**-H and C**7**-H_2 and between C**6**-H and C**10**-H. The major diastereomer was determined unambiguously by X-ray crystallography.*



(1*R, 6a*R**, 10a*S**) and (1*S**, 6a*R**, 10a*S**)-1-Ethyl-6-phenyl-2,3,6a,7-tetrahydro-1*H*,5*H*-benzo[d]pyrrolo[1,2-c]imidazole-5,8(6*H*)-dione (11g)**



A solution of 4-ethyl-1-azaspiro[4.5]deca-6,9-dien-8-one trifluoroacetate (45.0 mg, 0.154 mmol) in anhydrous CH_2Cl_2 (0.77 mL, 0.2 M) was cooled to 0 °C and phenyl isocyanate (34.0 µL, 0.308 mmol) and Et_3N (86.0 µL, 0.618 mmol) was added. The reaction was stirred at this temperature for 2 h before warming to r.t. and stirring overnight, monitoring by TLC. Upon completion, the reaction mixture was quenched with sat. aq. NH_4Cl (1 mL) and extracted with EtOAc (3 × 5 mL). The combined organic extracts were washed with brine (5 mL), dried over Na_2SO_4, filtered and concentrated *in vacuo*. Purification by flash column chromatography (33 % EtOAc/hexane) afforded **11g** (34.1 mg, 75 %) as a colorless solid. A mixture of diastereomers A and B were obtained in a 4:1 ratio.

R_f = 0.6 (3 % MeOH/CH_2Cl_2); ν_{max} / cm^{-1} (solid) 2965 (m), 2926 (m), 2885 (m), 1692 (s), 1683 (s), 1380 (s), 1309 (s); HRMS (ESI^+) Calculated for $C_{18}H_{20}N_2NaO_2$: 319.1417. Found $[M+Na]^+$: 319.1426.

Data for the major diastereomer A: m.p.: 148 - 151 °C (EtOAc/hexane); ^1H NMR (400 MHz, $CDCl_3$) δ 7.37 - 7.30 (4H, m, PhC<u>H</u>), 7.17 - 7.11 (1H, m, PhC<u>H</u>), 6.57 (1H, d, *J* = 10.3 Hz, C**7**-<u>H</u>), 6.21 (1H, d, *J* = 10.3 Hz, C**8**-<u>H</u>), 4.57 (1H, app. t, *J* = 6.2 Hz, C**11**-<u>H</u>), 3.87 - 3.78 (1H, m, C**1**-<u>H</u>), 3.43 - 3.35 (1H, m, C**1**-<u>H</u>'), 2.84 (1H, dd, *J* = 16.3, 5.8 Hz, C**10**-<u>H</u>), 2.66 (1H, dd, *J* = 16.3, 7.0 Hz, C**10**-<u>H</u>'), 2.45 - 2.36 (1H, m, C**2**-<u>H</u>), 2.08 - 1.98 (1H, m, C**3**-<u>H</u>), 1.88 - 1.76 (1H, m, C**2**-<u>H</u>'), 1.54 - 1.44 (1H, m, C**4**-<u>H</u>), 1.39 - 1.28 (1H, m, C**4**-<u>H</u>'), 0.99 (3H, t, *J* = 7.4 Hz, C**5**-<u>H</u>$_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.6 (C**9**), 159.4 (C**14**), 142.4 (C**7**), 137.3 (Ph<u>C</u>), 129.6

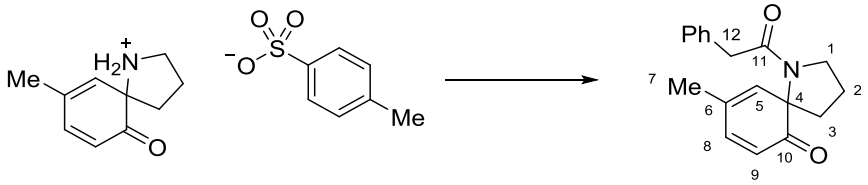
(C**8**), 129.3 (PhCH), 125.1 (PhCH), 122.2 (PhCH), 64.8 (C**6**), 58.6 (C**12**), 50.1 (C**3**), 43.9 (C**1**), 39.6 (C**11**), 30.9 (C**2**), 25.6 (C**4**), 13.2 (C**5**).

The minor diastereomer could not be isolated in a pure form.

Data for minor diastereomer B: *Charateristic peaks only*: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.48 (1H, d, *J* = 10.2 Hz, C**7**-H), 6.14 (1H, d, *J* = 10.2 Hz, C**8**-H), 4.51 - 4.48 (1H, m, C**11**-H), 3.94 - 3.87 (1H, m, C**1**-H), 3.20 (1H, td, *J* = 11.5, 5.0 Hz, C**1**-H'), 2.78 (1H, dd, *J* = 17.7, 2.8 Hz, C**10**-H), 2.57 (1H, dd, *J* = 17.5, 4.8 Hz, C**10**-H'), 1.05 (3H, t, *J* = 7.3 Hz, C**5**-H_3).

*The relative stereochemistry of the major diastereomer of this compound was determined by nOe experiments as indicated on the compound structure. nOes were observed between C**3**-H and C**11**-H and between C**4**-H_2 and C**7**-H.*

9-Methyl-1-(2-phenylacetyl)-1-azaspiro[4.5]deca-7,9-dien-6-one

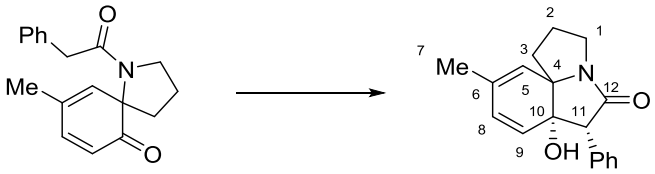


7k

The title compound was prepared using the dame procedure as for **9a** employing 9-Methyl-1-azaspiro[4.5]deca-7,9-dien-6-one tosylate (0.150 mmol), phenylacetyl chloride (40.0 μL, 0.300 mmol) and K_3PO_4 (127.4 mg, 0.600 mmol) in anhydrous THF (0.75 mL). Purification by flash column chromatography (EtOAc) afforded the title compound (34.0 mg, 81 %) as a 9:1 mixture of rotamers *A*:*B* and as a yellow oil; R_f = 0.4 (3 % MeOH/CH_2Cl_2); ν_{max} / cm^{-1} (film) 2972 (m), 2878 (m), 1675 (s), 1642 (s), 1406 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 - 7.27 (2H, m, PhCH, *A*+*B*), 7.25 - 7.20 (2.90H, m, PhCH, *A*+*B*), 7.13 - 7.09 (0.10H, m, 0.10 × PhCH, *B*), 6.93 (0.10H, dd, *J* = 9.8, 2.4 Hz, 0.10 × C**8**-H, *B*), 6.82 (0.90H, dd, *J* = 9.9, 2.4 Hz, 0.90 × C**8**-H, *A*), 6.18 - 6.09 (1.10H, m, 1.00 × C**9**-H, *A*+*B*, 0.10 × C**5**-H, *B*), 5.90 - 5.87 (0.90H, m, 0.90 × C**5**-H, *A*), 3.97 - 3.91 (0.10 H, m, 0.1 × C**1**-H, *B*), 3.78 - 3.69 (0.9H, m, 0.90 × C**1**-H, *A*), 3.67 - 3.60 (2.8H, m, 1.00 × C**1**-H', *A*+*B*, 1.80 × C**12**-H_2, *A*), 3.12 (0.20H, m, 0.20 × C**12**-H_2, *B*), 2.28 - 2.22 (0.10H, m, 0.10 × C**3**-H, *B*), 2.21 - 2.12 (1H, m, 0.90 × C**2**-H, *A*, C**3**-H', *B*), 2.10 - 1.95 (2.30 H, m, 1.00 × C**3**-H', *A*+*B*, 1.00 × C**2**-H', *A*+*B*, 0.30 × C**7**-H_3, *B*), 1.92 (2.70H, s, C**7**-H_3, *A*), 1.89 - 1.82 (1H, m, 0.90 × C**3**-H, *A*, 0.10 × C**2**-H, *B*); ^{13}C NMR (101 MHz, $CDCl_3$) δ

208. 6 (C**10**, *B*), 200.1 (C**10**, *A*), 170.3 (C**11**, *B*), 168.6 (C**11**, *A*), 145.5 (C**8**, *B*), 145.0 (C**8**, *A*), 140.3 (C**5**, *B*), 137.5 (C**5**, *A*), 134.5 (PhC, *A*+*B*), 129.6 (2 × PhCH, *B*), 129.2 (2 × PhCH, *A*), 128.7 (2 × PhCH, *A*), 128.3 (2 × PhCH, *B*), 126.8 (PhCH, *A*), 126.6 (PhCH, *B*), 125.8 (C**9**), 125.1 (C**9**, *B*), 70.1 (C**4**, *B*), 69.3 (C**4**, *A*), 49.0 (C**1**, *B*), 48.8 (C**1**, *A*), 41.9 (C**12**, *A*), 40.7 (C**12**, *B*), 40.3 (C**3**, *B*), 37.6 (C**3**, *A*+*B*), 24.0 (C**2**, *A*), 21.1 (C**7**, *A*), 20.9 (C**7**, *B*); HRMS (ESI$^+$) Calculated for $C_{18}H_{19}NNaO_2$: 304.1308. Found $[M+Na]^+$: 304.1318.

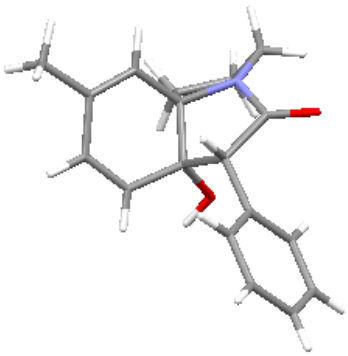
(6*R, 6a*S**)-6a-Hydroxy-9-methyl-6-phenyl-2,3,6,6a-tetrahydro-1*H*,5*H*-pyrrolo[2,1-i]indol-5-one (12k)**



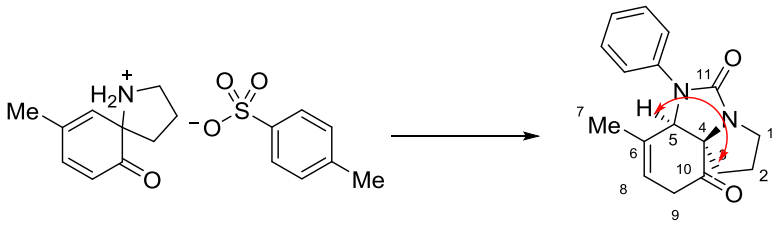
12k

The title compound was prepared using the same procedure as for **10a** employing 9-methyl-1-(2-phenylacetyl)-1-azaspiro[4.5]deca-7,9-dien-6-one (28.1 mg, 0.10 mmol) and 1.5 eq. lithium bis(trimethylsilyl)amide (1.0 M in THF) in anhydrous THF (1 mL). Purification by flash column chromatography afforded **12k** (18.9 mg, 67 %, > 15:1 d.r.) as a colorless solid; m.p.: 150 - 152 ^{o}C (EtOAc/hexane); R_f = 0.5 (3% MeOH/CH_2Cl_2); ν_{max} / cm^{-1} (solid) 3356 (br m), 2969 (m), 2942 (m), 2880 (m), 1673 (s), 1402 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 - 7.31 (3H, m, PhCH), 7.28 - 7.24 (2H, m, PhCH), 5.78 (1H, dd, *J* = 9.8, 1.5 Hz, C**8**-H), 5.53 (1H, m, C**5**-H), 5.38 (1H, d, *J* = 9.8 Hz, C**9**-H), 4.27 (1H, s, C**11**-H), 3.89 (1H, ddd, *J* = 12.1, 7.7, 4.7 Hz, C**1**-H), 3.16 (1H, ddd, *J* = 11.8, 7.7, 1.3 Hz, C**1**-H'), 2.54 (1H, ddd, *J* = 12.9, 8.4, 6.1 Hz, C**3**-H), 2.07 - 1.97 (1H, m, C**2**-H), 1.95 - 1.87 (1H, m, C**2**-H'), 1.85 (1H, d, *J* = 1.5 Hz, C**7**-H_3), 1.44 (1H, dt, *J* = 12.9, 7.3 Hz, C**3**-H'); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.8 (C**12**), 134.2 (2 × PhCH), 131.3 (C**9**), 131.2 (PhC), 128.6 (2 × PhCH), 128.6 (C**6**), 128.0 (PhCH), 127.0 (C**5**), 126.7 (C**8**), 79.1 (C**10**), 72.7 (C**4**), 61.6 (C**11**), 42.9 (C**1**), 30.6 (C**3**), 26.2 (C**2**), 21.2 (C**7**); HRMS (ESI$^+$) Calculated for $C_{18}H_{19}NNaO_2$: 304.1308. Found $[M+Na]^+$: 304.1322.

The relative stereochemistry of this compound was determined unambiguously using X-ray crystallography.



(6a*R*, 10a*R***)7-Methyl-6-phenyl-2,3,6a,9-tetrahydro-1*H*,5*H*-benzo[d]pyrrolo[1,2-c]imidazole-5,10(6*H*)-dione (11k)**

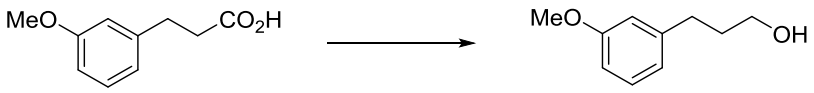


A solution of 9-Methyl-1-azaspiro[4.5]deca-7,9-dien-6-one tosylate (**7k**) (0.15 mmol) in anhydrous CH_2Cl_2 (0.2 M) was cooled to 0 °C and 1.1 eq. phenyl isocyanate (18 µL, 0.17 mmol) and Et_3N (84 µL, 0.60 mmol) were added. The reaction was stirred at this temperature for 3 h then heated to 40 °C and stirred overnight, monitoring by TLC analysis. Upon completion, the reaction mixture was cooled to r.t., quenched with sat. aq. NH_4Cl (1 mL) and extracted with EtOAc (3 × 5 mL). The combined organic phases were washed with brine (5 mL), dried over Na_2SO_4, filtered and concentrated *in vacuo*. Purification by flash column chromatography (1% MeOH/CH_2Cl_2) afforded **11k** (28.9 mg, 68 %) as a colorless solid; m.p.: 110 - 113 °C (EtOAc/hexane); R_f = 0.6 (3 % MeOH/CH_2Cl_2); ν_{max} / cm^{-1} (solid) 2987 (m), 2953 (m), 2923 (m), 1726 (s), 1693 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 - 7.35 (4H, m, PhC<u>H</u>), 7.21 - 7.16 (1H, m, PhC<u>H</u>), 5.59 - 5.55 (1H, m, C**8**-<u>H</u>), 4.74 (1H, s, C**5**-<u>H</u>), 3.94 - 3.87 (1H, m, C**1**-<u>H</u>), 3.68 - 3.60 (1H, m, C**9**-<u>H</u>), 2.88 (1H, ddd, *J* = 12.2, 9.0, 6.5 Hz, C**1**-<u>H</u>'), 2.79 - 2.70 (2H, m, C**9**-<u>H</u>', C**3**-<u>H</u>), 2.00 - 1.85 (2H, m, C**2**-<u>H</u>$_2$), 1.55 - 1.46 (1H, m, C**3**-<u>H</u>'), 1.41 (3H, s, C**7**-<u>H</u>$_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 204.6 (C**10**), 161.5 (C**11**), 138.9 (Ph<u>C</u>), 134.4 (C**6**), 129.3 (2 × Ph<u>C</u>H), 125.8 (Ph<u>C</u>H), 123.9 (2 × Ph<u>C</u>H), 121.6 (C**8**), 70.9 (C**4**), 66.5 (C**5**), 45.9 (C**1**), 36.5

(C**9**), 29.4 (C**3**), 23.7 (C**2**), 22.6 (C**7**); HRMS (ESI$^+$) Calculated for $C_{17}H_{18}N_2NaO_2$: 305.1260. Found $[M+Na]^+$: 305.1273.

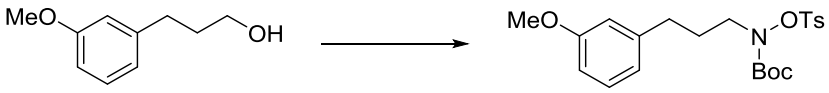
*The relative stereochemistry was determined using nOe analysis as indicated on the compound structure. An nOe was observed between C**5**-H and C**3**-H$_2$.*

3-(3-Methoxyphenyl)propan-1-ol[1]



General procedure 2: 3-(3-Methoxyphenyl)propanoic acid (0.54 g, 3.00 mmol) and 2.0 eq. $LiAlH_4$ (1 M in THF) in anhydrous Et_2O were employed to afford the title compound (0.34 mg, 68 %) as a pale yellow oil which was used without further purification; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 - 7.19 (1H, m), 6.82 - 6.79 (1H, m), 6.77 - 6.73 (2H, m), 3.80 (3H, s), 3.66 (2H, t, *J* = 6.5 Hz), 2.71 - 2.67 (2H, m), 2.14 (1H, br s), 1.92 - 1.85 (2H, m). *Spectroscopic properties were consistent with the data available in the literature.*[1]

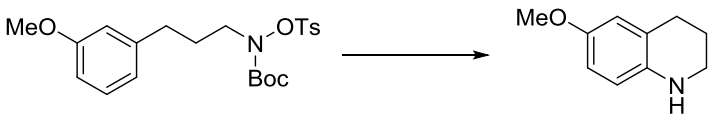
***tert*-Butyl (3-(3-methoxyphenyl)propyl)(tosyloxy)carbamate (13a)**[1]



13a

General procedure C: 3-(3-Methoxyphenyl)propan-1-ol (0.24 mg, 1.50 mmol), PPh_3 (0.47 mg, 1.80 mmol), DIAD (0.35 mL, 1.80 mmol) and TsONHBoc (517 mg, 1.80 mmol) in anhydrous THF (8 mL) were employed. Purification by flash column chromatography (gradient, eluent 5 - 10% EtOAc/hexane) afforded **13a** (0.53 g, 81 %) as a colorless, viscous oil; R_f = 0.5 (33% EtOAc/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (2H, d, *J* = 8.4 Hz), 7.32 (2H, d, *J* = 8.4 Hz), 7.19 (1H, t, *J* = 7.8 Hz), 6.80 - 6.69 (3H, m), 3.79 (3H, s), 3.62 (2H, br s), 2.57 (2H, t, *J* = 7.8 Hz), 2.44 (3H, s), 1.95 (2H, br s), 1.21 (9H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.7, 155.4, 145.7, 142.7, 131.2, 129.7, 129.5, 129.4, 120.7, 113.9, 111.4, 83.2, 55.1, 52.6, 32.8, 27.6, 27.3, 21.7. *Spectroscopic properties were consistent with the data available in the literature.*[1]

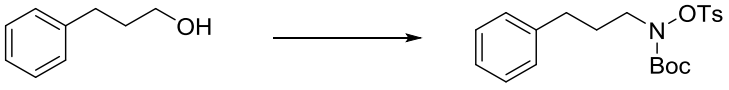
6-Methoxy-1,2,3,4-tetrahydroquinoline (14a)[1]



13a **14a**

General procedure E: *tert*-Butyl (3-(3-methoxyphenyl)propyl)(tosyloxy)carbamate (**13a**) (87.1 mg, 0.20 mmol), TFA (31.0 μL, 0.40 mmol) in TFE (2 mL) were employed. After stirring at r.t. for 40 h, purification by flash column chromatography (gradient, eluent 10 - 25% EtOAc/hexane) afforded **14a** (26.0 mg, 80 %) as a pale yellow oil; R_f = 0.45 (33 % EtOAc/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.63 - 6.54 (2H, m), 6.46 (1H, d, *J* = 8.5 Hz), 3.73 (3H, s), 3.37 (1H, br s), 3.27 - 3.24 (2H, m), 2.76 (2H, t, *J* = 6.5 Hz), 1.97 - 1.89 (2H, m); ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.9, 138.8, 122.9, 115.6, 114.9, 112.9, 55.8, 42.3, 27.2, 22.4. *Spectroscopic properties were consistent with the data available in the literature.*[1]

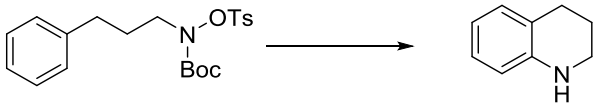
***tert*-Butyl (3-phenylpropyl)(tosyloxy)carbamate (13b)**[1]



13b

General procedure C: 3-Phenylpropan-1-ol (0.20 g, 1.50 mmol), PPh_3 (0.47 g, 1.80 mmol), DIAD (0.36 mL, 1.80 mmol) and TsONHBoc (0.52 g, 1.80 mmol) in anhydrous THF (6 mL) were employed. Purification by flash column chromatography (10 % EtOAc/hexane) afforded **13b** (0.52 g, 85 %) as a viscous colorless oil; R_f = 0.7 (33% EtOAc/hexane); ν_{max} / cm^{-1} (film) 2981 (m), 2932 (m), 2865 (m), 1718 (s), 1598 (m), 1454 (m), 1368 (s), 1294 (m), 1191 (s), 1151 (s), 1177 (s), 1089 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (2H, d, *J* = 8.3 Hz), 7.35 - 7.31 (2H, m), 7.31 - 7.26 (2H, m), 7.22 - 7.15 (3H, m), 3.63 (2H, br s), 2.60 (2H, t, *J* = 7.8 Hz), 2.45 (3H, s), 2.02 - 1.91 (2H, m), 1.23 (9H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.4, 145.7, 141.1, 131.2, 129.7, 129.5, 128.4, 128.3, 126.0, 83.2, 52.6, 32.8, 27.6, 27.4, 21.7. *Spectroscopic properties were consistent with the data available in the literature.*[1]

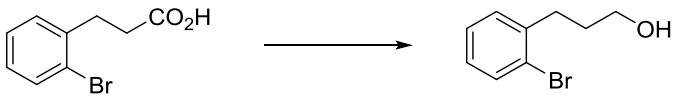
1,2,3,4-Tetrahydroquinoline (14b)[1]



13b **14b**

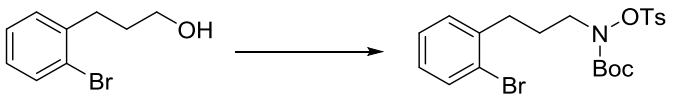
General procedure E: *tert*-Butyl (3-phenylpropyl)(tosyloxy)carbamate (**13b**) (0.12 g, 0.30 mmol) and TFA (46.0 μL, 0.60 mmol) in TFE (3 mL) were employed. After stirring at r.t. for 24 h, purification by flash column chromatography (33 % Et_2O/hexane) afforded **14b** (26.0 mg, 65 %) as a yellow oil; R_f = 0.7 (33% EtOAc/hexane); ν_{max}/cm^{-1} (film); ^1H NMR (400 MHz, $CDCl_3$) δ 6.99 - 6.95 (2H, m), 6.62 (1H, t, *J* = 7.3 Hz), 6.48 (1H, d, *J* = 7.9 Hz), 3.80 (1H, br s), 3.31 (2H, t, *J* = 5.4 Hz), 2.78 (2H, t, *J* = 6.5 Hz), 2.01 - 1.90 (2H, m); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.8, 129.5, 126.7, 121.4, 116.9, 114.2, 41.9, 26.9, 22.2. *Spectroscopic properties were consistent with the data available in the literature.*[1]

3-(2-Bromophenyl)propan-1-ol[1]



To a solution of ethyl 3-(2-bromophenyl)propanoic acid (0.92 g, 4.00 mmol) in anhydrous THF (20 mL) at -10 ºC was added 0.75 eq. $LiAlH_4$ (1 M in THF) and the reaction was stirred at the same temperature for 30 min. To the reaction mixture was added water (0.5 mL), aq. 1 M NaOH (0.2 mL) and a further portion of water (1 mL). The reaction mixture was warmed to room temperature, filtered through Celite® and washed with CH_2Cl_2. The phases were separated and the aqueous phase washed with CH_2Cl_2. The combined organic extracts were dried over Na_2SO_4, filtered and concentrated *in vacuo* to afford the title compound as a colorless oil (0.16 g, 19 %) which was used without further purification; ^1H NMR (400 MHz, $CDCl_3$) δ 7.53 (1H, d, *J* = 8.0 Hz), 7.26 - 7.21 (2H, m), 7.09 - 7.02 (1H, m), 3.70 (2H, t, *J* = 6.4 Hz), 2.83 (2H, t, *J* = 7.80 Hz), 1.94 - 1.85 (2H, m), 1.54 (1H, br s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.1, 132.8, 130.4, 127.6, 127.5, 124.4, 62.1, 32.7, 32.4. *Spectroscopic properties were consistent with the data available in the literature.*[1]

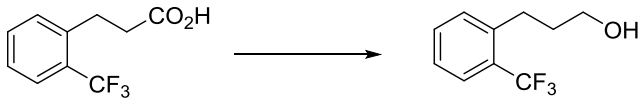
***tert*-Butyl(3-(2-bromophenyl)propyl)(tosyloxy)carbamate (13c)**[1]



13c

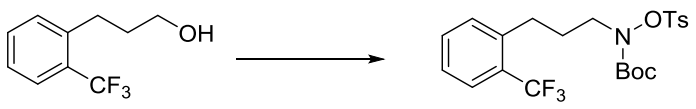
General procedure C: 3-(2-Bromophenyl)propan-1-ol (0.16 g, 0.74 mmol), PPh_3 (0.23 g, 0.88 mmol), DIAD (0.17 mL, 0.88 mmol) and TsONHBoc (0.25 g, 0.88 mmol) in anhydrous THF (4 mL) were employed. Purification by flash column chromatography (10 % EtOAc/hexane) afforded **13c** (0.26 g, 72 %) as a colorless solid; R_f = 0.6 (20 % EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (2H, d, *J* = 8.3 Hz), 7.52 (2H, dd, *J* = 7.9, 1.1 Hz), 7.33 (2H, d, *J* = 8.1 Hz), 7.24 - 7.19 (2H, m), 7.06 (1H, ddd, *J* = 7.9, 6.6, 2.4 Hz), 3.66 (2H, br s), 2.71 (2H, t, *J* = 7.9 Hz), 2.45 (3H, s), 1.99 - 1.90 (2H, m), 1.23 (9H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.5, 145.8, 140.6, 132.9, 131.4, 130.3, 129.8, 129.7, 127.9, 127.6, 124.5, 83.4, 52.7, 33.3, 27.8, 26.2, 21.9. *Spectroscopic properties were consistent with the data available in the literature*.[1]

3-(2-(Trifluoromethyl)phenyl)propan-1-ol[1]



General procedure E: 3-(2-(Trifluoromethyl)phenyl)propanoic acid (0.55 g, 2.50 mmol) and 1.0 eq. $LiAlH_4$ (1.0 M in THF) in anhydrous THF were employed to afford the title compound (0.38 g, 75 %) as a colorless oil which was used without further purification; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (1H, d, *J* = 7.9 Hz), 7.45 (1H, t, *J* = 7.6 Hz), 7.34 (1H, d, *J* = 7.7 Hz), 7.27 (1H, t, *J* = 7.6 Hz), 3.71 (2H, t, *J* = 6.4 Hz), 2.87 (2H, t, *J* = 7.9 Hz), 1.93 (1H, br s), 1.92 - 1.85 (2H, m); ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.7, 131.7, 131.0, 128.5, 125.9, 123.3, 120.6, 62.2, 34.5, 28.9. *Spectroscopic properties were consistent with the data available in the literature.*[1]

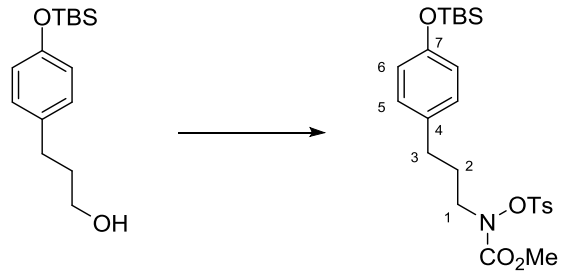
***tert*-Butyl (tosyloxy)(3-(2-(trifluoromethyl)phenyl)propyl)carbamate (13d)**[1]



3d

General procedure C: 3-(2-(Trifluoromethyl)phenyl)propan-1-ol (0.20 g, 1.00 mmol), PPh_3 (0.32 g, 1.20 mmol), DIAD (0.24 mL, 1.20 mmol) and TsONHBoc (0.35 mg, 1.20 mmol) in anhydrous THF (5 mL) were employed. Purification by flash column chromatography (10% EtOAc/hexane) afforded **3d** (0.45 mg, 95 %) as a colorless oil; R_f = 0.5 (20 % EtOAc/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (2H, d, *J* = 8.3 Hz), 7.60 (2=1H, d, *J* = 7.9 Hz), 7.47 (1H, t, *J* = 7.6 Hz), 7.33 (2H, d, *J* = 8.3 Hz), 7.31 - 7.27 (1H, m), 3.67 (2H, br s), 2.75 (2H, t, *J* = 8.1 Hz), 2.44 (3H, s), 2.01 - 1.90 (2H, m), 1.23 (9H, s); ^{13}C NMR (101 MHz, $CDCl_2$) δ 155.5, 145.8, 140.1, 132.0, 131.3, 130.9, 129.8, 129.7, 128.5, 126.3, 126.1, 83.5, 52.9, 29.7, 27.9, 27.7, 21.8. *Spectroscopic properties were consistent with the data available in the literature*.[1]

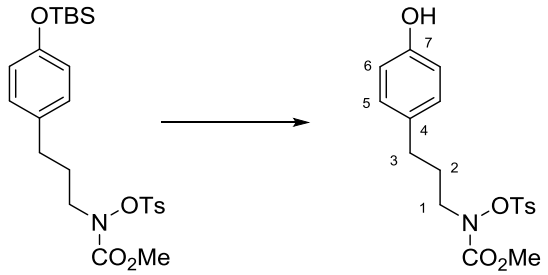
Methyl (3-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)propyl)(tosyloxy)carbamate



General procedure C: 3-(4-((*tert*-Butyldimethylsilyl)oxy)phenyl)propan-1-ol (0.53 g, 2.00 mmol), PPh_3 (0.63 g, 2.40 mmol), DIAD (0.47 mL, 2.40 mmol) and methyl (tosyloxy)carbamate (0.59 g, 2.40 mmol) in anhydrous THF (8 mL) were employed. Purification by flash column chromatography (10 % EtOAc/hexane) afforded the title compound (0.93 g, 94 %) as a colorless oil; R_f = 0.4 (20 % EtOAc/hexane); ν_{max} / cm^{-1} (film) 2955 (m), 2930 (m), 2858 (m), 1728 (s), 1509 (s), 1253 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (2H, d, *J* = 8.1 Hz, Ts ArC<u>H</u>), 7.33 (2H, d, *J* = 8.1 Hz, Ts ArC<u>H</u>), 6.99 (2H, d, *J* = 8.1 Hz, C**5**-<u>H</u>), 6.74 (2H, d, *J* = 8.1 Hz, C**6**-<u>H</u>), 3.58 (2H, app. br s, C**1**-$\underline{H}_2$), 3.47 (3H, s, OC$\underline{H}_3$), 2.51 (2H, t, *J* = 7.8 Hz, C**3**-$\underline{H}_2$), 2.45 (3H, s, Ts C$\underline{H}_3$), 1.94 - 1.85 (2H, m, C**2**-$\underline{H}_2$), 0.98 (9H, s, TBS (C$\underline{H}_3$)$_3$), 0.18 (6H, s, TBS Si(C$\underline{H}_3$)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.2 (C=O), 153.9 (C**7**), 146.0 (Ts Ar<u>C</u>), 133.6 (C**4**), 131.2 (Ts Ar<u>C</u>), 129.7 (2 x Ts Ar<u>C</u>H), 129.6 (2 x Ts Ar<u>C</u>H), 129.2

(C**5**), 120.1 (C**6**), 53.7 (O<u>C</u>H_3), 52.7 (C**1**), 32.0 (C**3**), 27.7 (C**2**), 25.8 (TBS (<u>C</u>H_3)$_3$), 21.9 (Ts <u>C</u>H_3), 18.3 (TBS Si<u>C</u>$(CH_3)_3$), -4.3 (TBS Si$(\underline{C}H_3)_2$); HRMS (ESI$^+$) Calculated for $C_{24}H_{35}NNaO_6SSi$: 516.1847. Found $[M+Na]^+$: 516.1851.

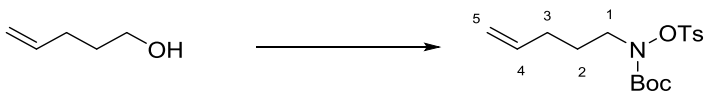
Methyl (3-(4-hydroxyphenyl)propyl)(tosyloxy)carbamate (15)



15

General procedure D: Methyl (3-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)propyl)(tosyloxy) carbamate (490 mg, 1.00 mmol) and 1.1 eq. 1:1 TBAF/AcOH solution (0.1 M in THF, 11 mL, 1.1 mmol) in THF (20 mL) were employed. Purification by flash column chromatography (gradient 20 – 33 % EtOAc/hexane) afforded **15** (289 mg, 76 %) as a viscous, colorless oil; R_f = 0.1 (20 % EtOAc/hexane); ν_{max} / cm^{-1} (film) 3431 (m, br), 3023 (m), 2956 (m), 1726 (m), 1514 (m), 1175 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (2H, d, *J* = 8.2 Hz, Ts ArC<u>H</u>), 7.33 (2H, d, *J* = 8.2 Hz, Ts ArC<u>H</u>), 6.99 (2H, d, *J* = 8.1 Hz, C**5**-<u>H</u>), 6.74 (2H, d, *J* = 8.1 Hz, C**6**-<u>H</u>), 4.88 (1H, s, O<u>H</u>), 3.59 (2H, br s, C**1**-$\underline{H}_2$), 2.51 (2H, t, *J* = 7.8 Hz, C**3**-$\underline{H}_2$), 2.45 (3H, s, OC<u>H</u>$_3$), 1.95 - 1.85 (2H, m, C**2**-$\underline{H}_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.3 (C=O), 154.0 (C**7**), 146.1 (Ts Ar<u>C</u>), 133.0 (C**4**), 131.1 (Ts Ar<u>C</u>), 129.7 (2 x Ts Ar<u>C</u>H), 129.6 (2 x Ts Ar<u>C</u>H), 129.5 (C**5**), 115.4 (C**6**), 53.8 (O<u>C</u>H_3), 52.7 (C**1**), 31.9 (C**3**), 27.8 (C**2**), 21.9 (Ts <u>C</u>H_3); HRMS (ESI$^+$) Calculated for $C_{18}H_{21}NNaO_6S$: 402.0982. Found $[M+Na]^+$: 402.0984.

***tert*-butyl pent-4-en-1-yl(tosyloxy)carbamate (17)**



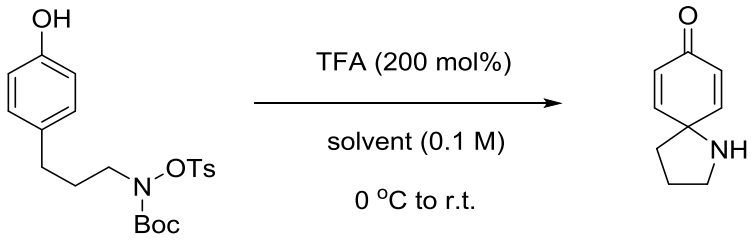
17

General procedure C: 4-Penten-1-ol (0.17 g, 2.00 mmol), PPh_3 (0.63 g, 2.40 mmol), DIAD (0.47 mL, 2.40 mmol) and TsONHBoc (0.69 g, 2.40 mmol) in anhydrous THF (15 mL) were

employed. Purification by flash column chromatography (10 % EtOAc/hexane) afforded **17** (0.47 g, 66%) as a colorless crystalline solid; m.p.: 47-50 °C (EtOAc/hexane); R_f = 0.5 (33% EtOAc/hexane); ν_{max} / cm^{-1} (film) 2977 (m), 1715 (s), 1365 (s), 1355 (s), 1177 (s), 1154 (s); ^1H NMR (400 MHz, $CDCl_3$) δ 7.85 (2H, d, *J* = 8.3 Hz, Ts ArC<u>H</u>), 7.34 (2H, d, *J* = 8.2 Hz, Ts ArC<u>H</u>), 5.81 - 5.71 (1H, m, C**4**-<u>H</u>), 5.05 - 4.93 (2H, m, C**5**-<u>H_2</u>), 3.62 (2H, app. br s, C**1**-<u>H_2</u>), 2.45 (3H, s, Ts C<u>H_3</u>), 2.07 - 2.00 (2H, m, C**3**-<u>H_2</u>), 1.77 - 1.66 (2H, m, C**2**-<u>H_2</u>), 1.22 (9H, s, Boc (C<u>H_3</u>)$_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.6 (Boc C=O), 145.8 (Ts Ar<u>C</u>), 137.4 (C**4**), 131.4 (Ts Ar<u>C</u>) 129.8 (Ts Ar<u>C</u>H), 129.7 (Ts Ar<u>C</u>H), 115.4 (C**5**), 52.6 (C**1**), 30.7 (C**3**), 27.7 (Boc (<u>C</u>H_3)$_3$), 25.0 (C**2**), 21.8 (Ts <u>C</u>H_3); HRMS (ESI^+) Calculated for $C_{17}H_{25}NNaO_5S$: 378.1346. Found $[M+Na]^+$: 378.1346.

Selected control reactions and solvent screen

Table 1. Solvent investigation

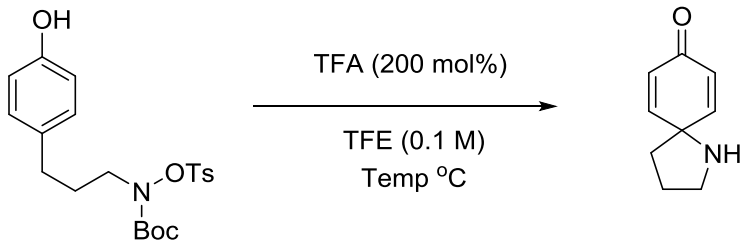


5a **7a**

Entry	Solvent (0.1 M)	Time (h)	Yield (%)[a]
1	TFE	24	77
2	EtOH	24	0
3	Toluene	24	40
4	THF	24	0
5	CH_2Cl_2	24	41
6	EtOAc	24	0
7	1,4-Dioxane	24	0
8	MeCN	24	8
9	2-propanol	24	0
10	MeOH	24	0

[a]In situ yield determined by ^1H NMR against 1,3,5-trimethoxybenzene internal standard.

Table 2. Effect of increased temperature on the reaction

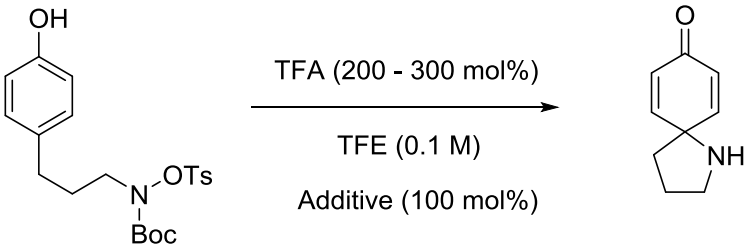


5a **7a**

Entry	Temp (°C)	Time	Yield (%)[a]
1	40	15 h	78
2	60	10 h	74
3	80	8 h	44

[a]In situ yield determined by ^{1}H NMR against 1,3,5-trimethoxybenzene internal standard.

Table 2. Results of investigation into possible radical based mechanism

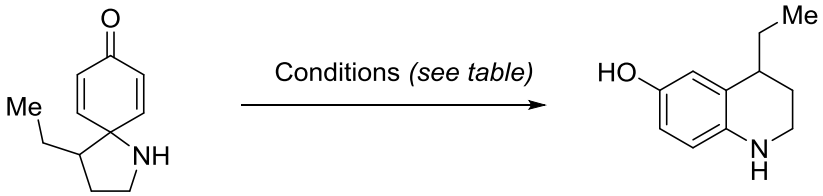


5a **7a**

Entry	TFA (mol%)	Additive (100 mol%)	Temp (°C)	Time (h)	Yield (%)[a]
1	200	none	0 - r.t.	24	77
2	200	none	0 - r.t.	24	79[b]
3	200	TEMPO	0 - r.t.	24	14
4	300	TEMPO	0 - r.t.	24	30
5	300	TEMPO	40	42	58
6	200	BHT	0 - r.t.	24	46
7	300	BHT	40	22	69
8	200	none	0 - r.t.	24	78[c]

[a]In situ yield determined by ^{1}H NMR against 1,3,5-trimethoxybenzene internal standard. [b]Reaction performed using distilled TFE and TFA. [c]Reaction performed in the absence of light.

Table 4. Dienone-phenol rearrangement control reactions

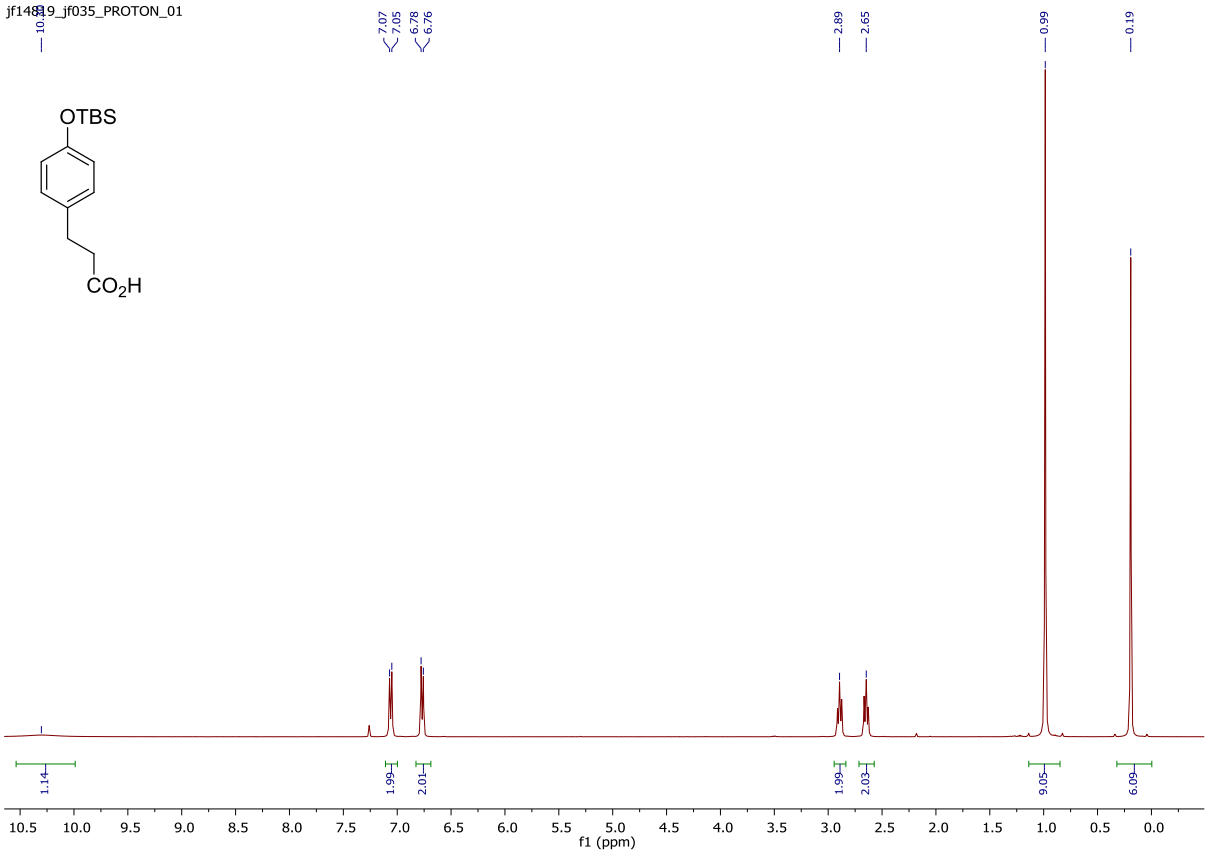


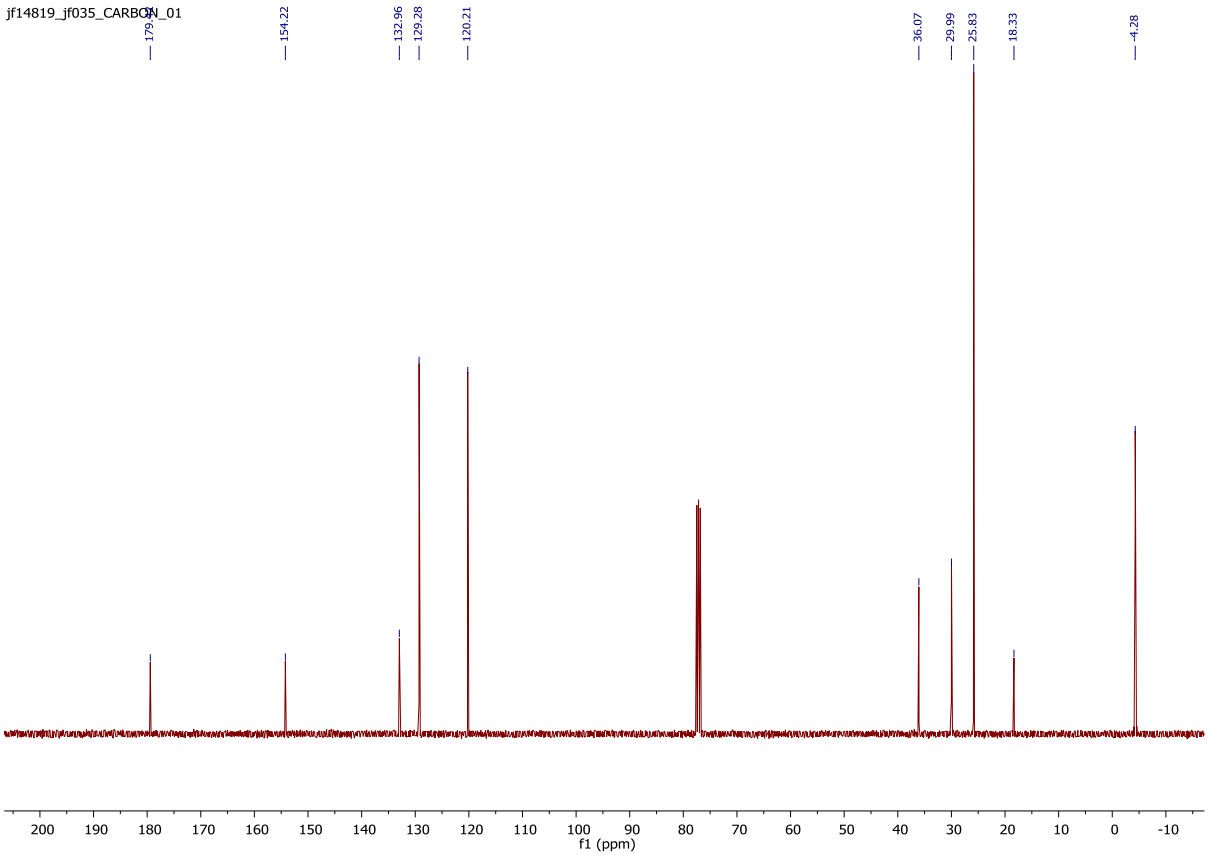
7g **8g**

Entry	TFA (mol%)	TFE (M)	Temp (°C)	Time (h)	Yield (%)[a]
1	15	0.1	r.t.	48	50
2	0	0.1	60	25	57

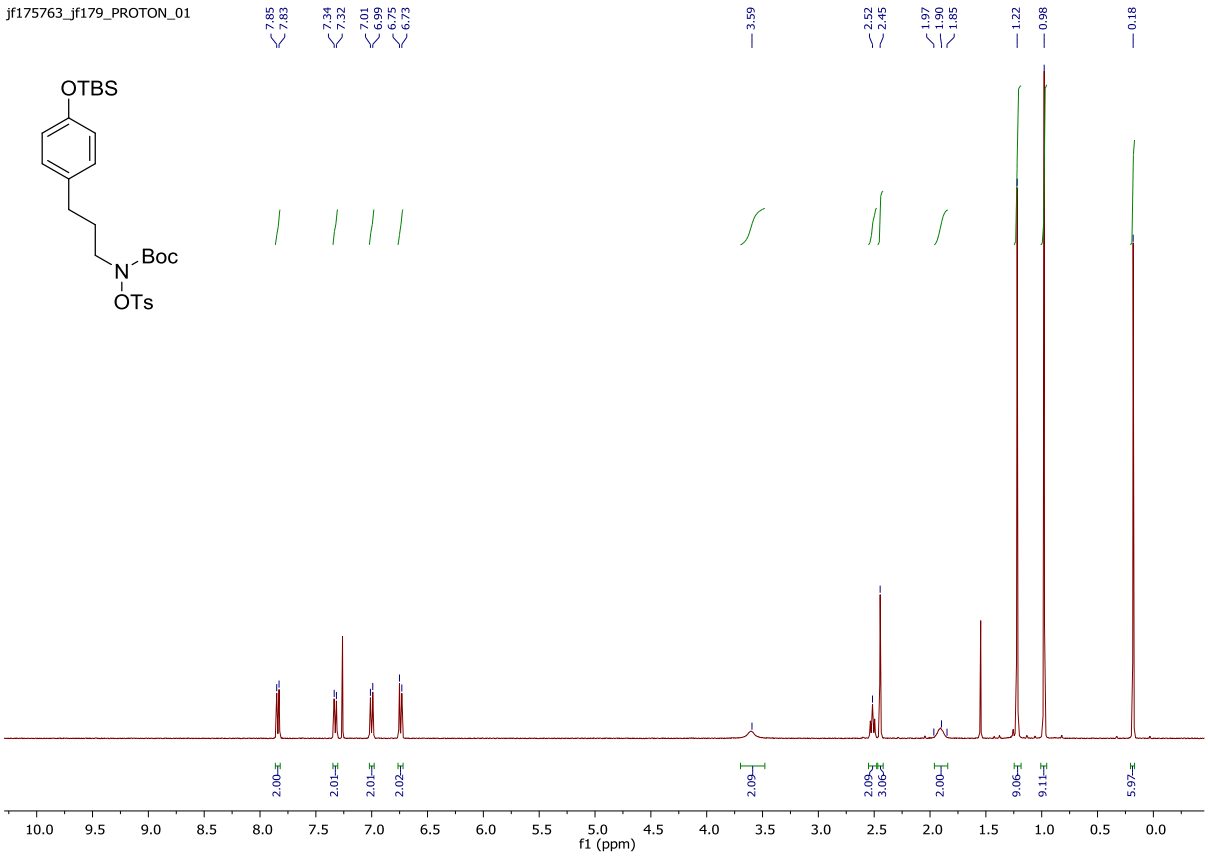
[a]In situ yield determined by ^{1}H NMR against 1,3,5-trimethoxybenzene internal standard.

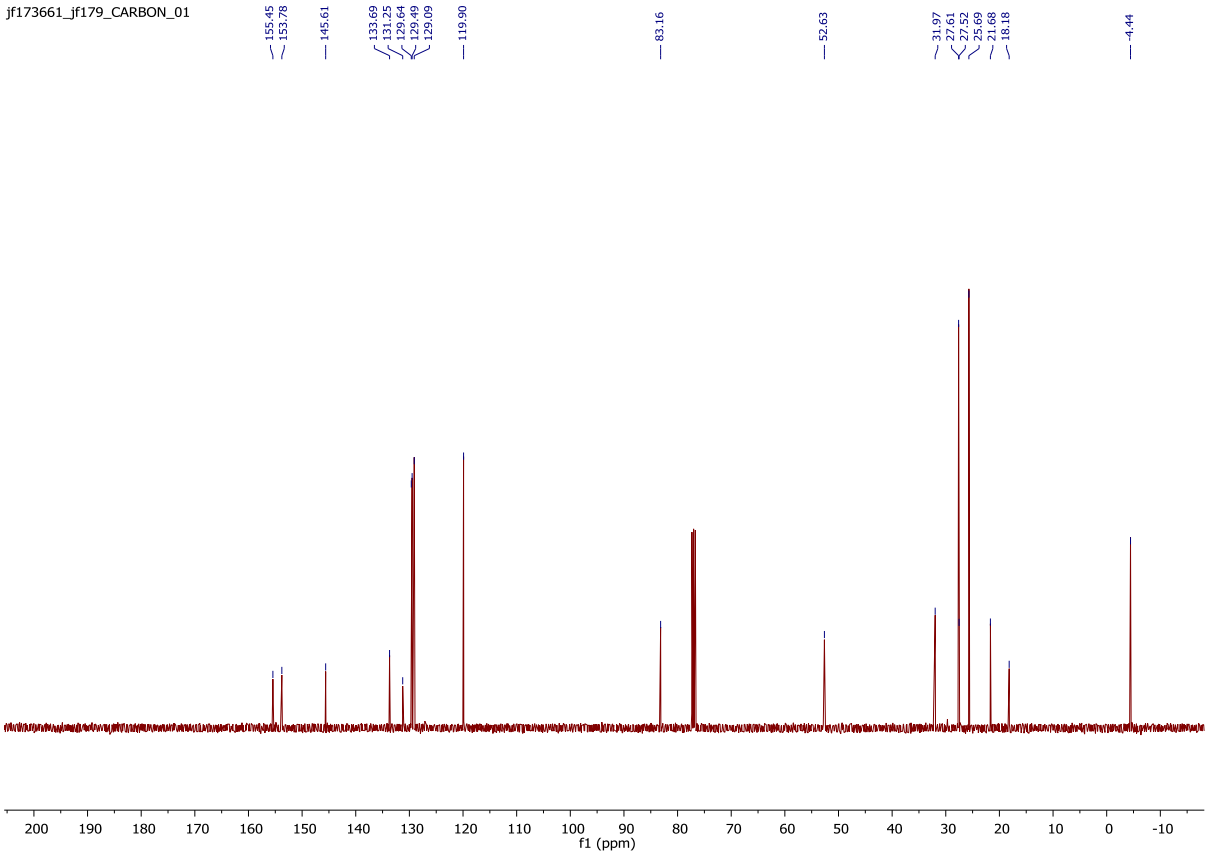
3-(4-((*tert*-Butyldimethylsilyl)oxy)phenyl)propanoic acid



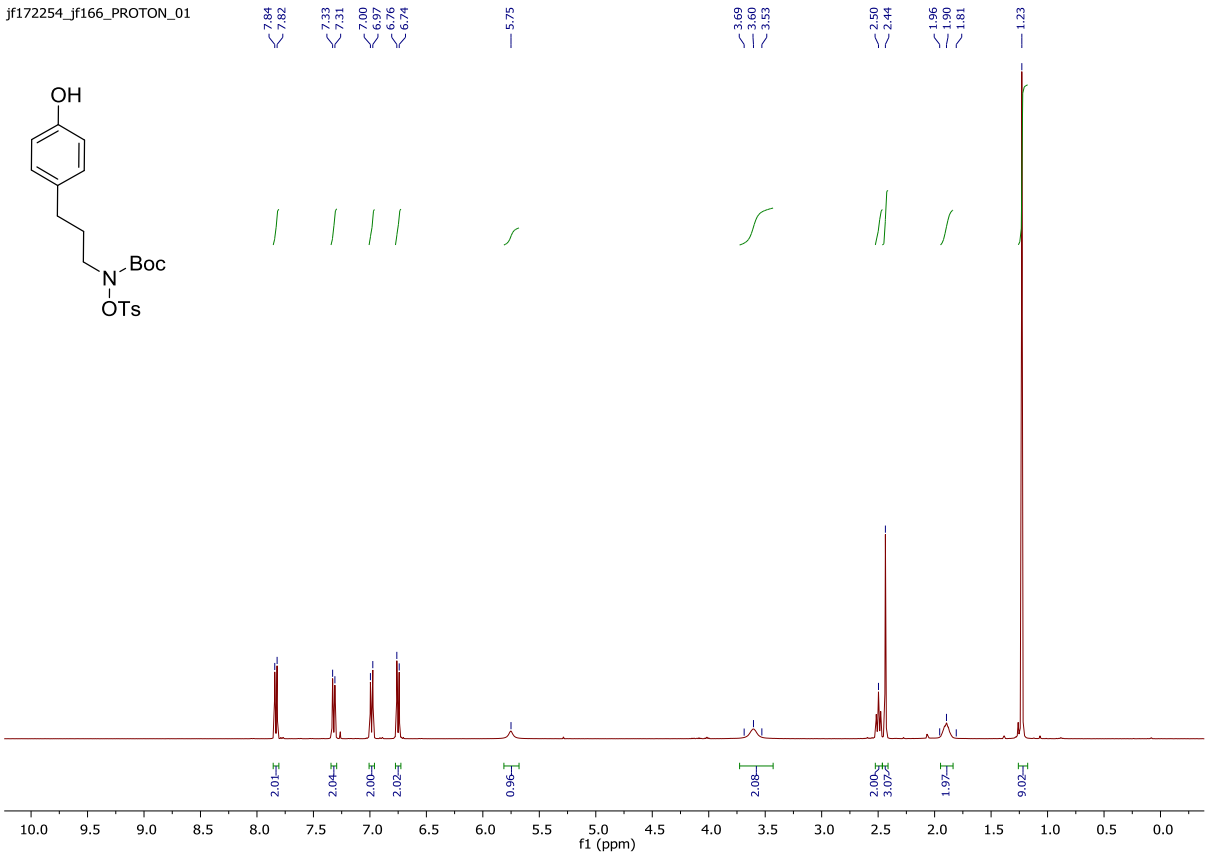


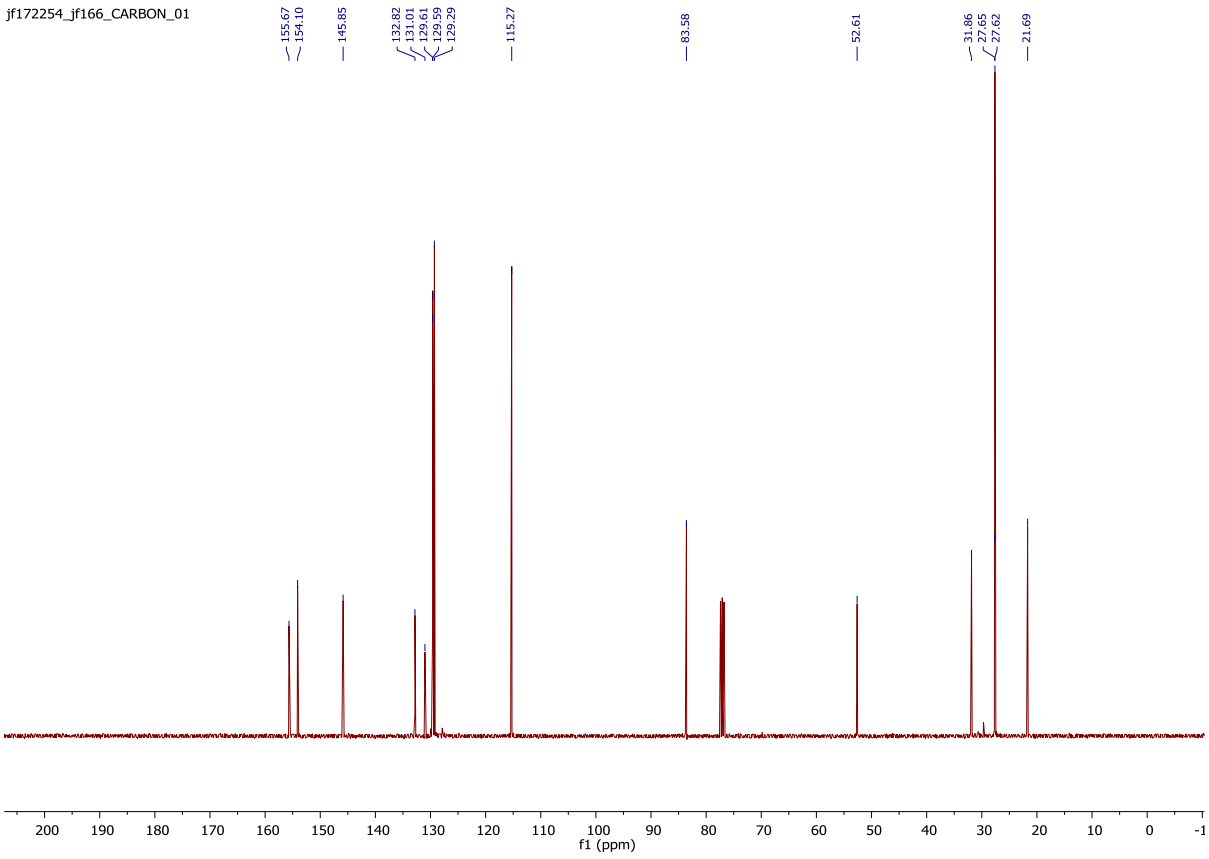
tert-Butyl (3-(4-((_tert_-butyldimethylsilyl)oxy)phenyl)propyl)(tosyloxy)carbamate (_silyl_-5a)



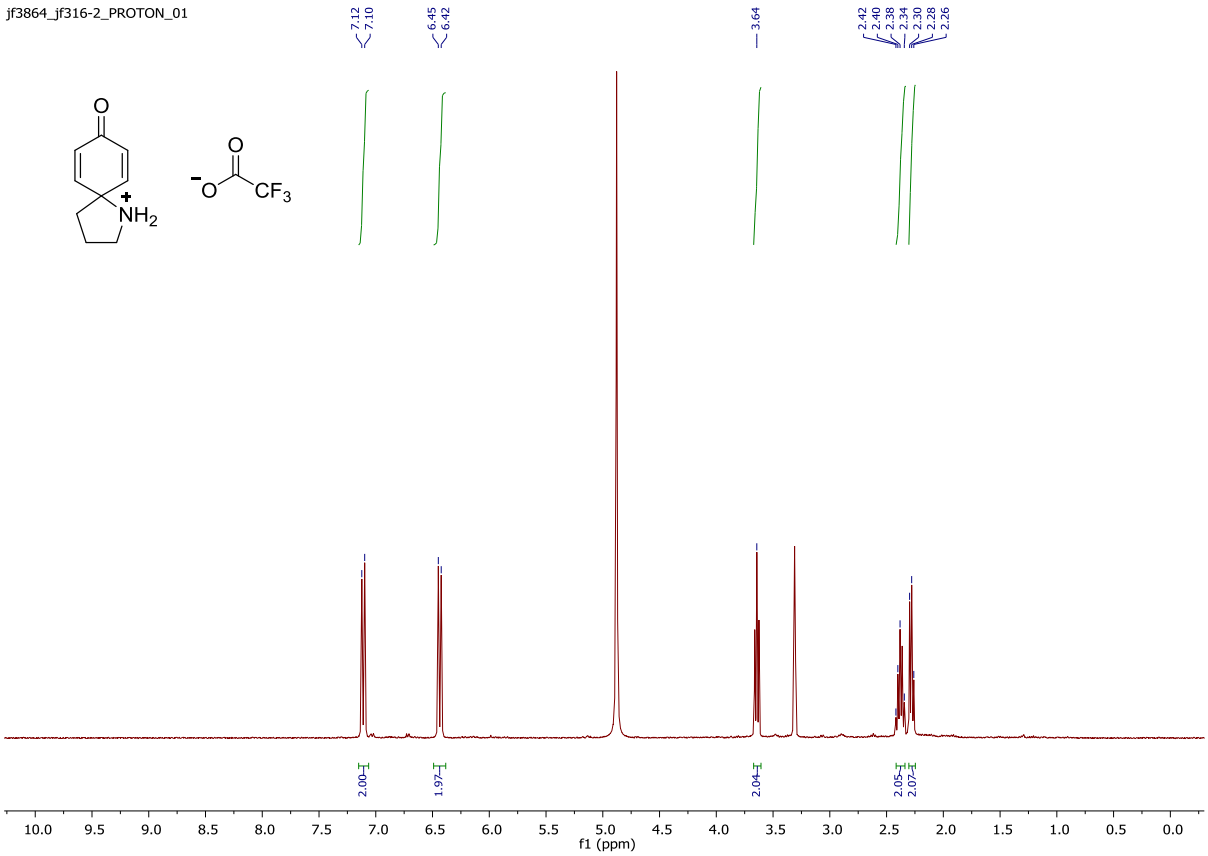


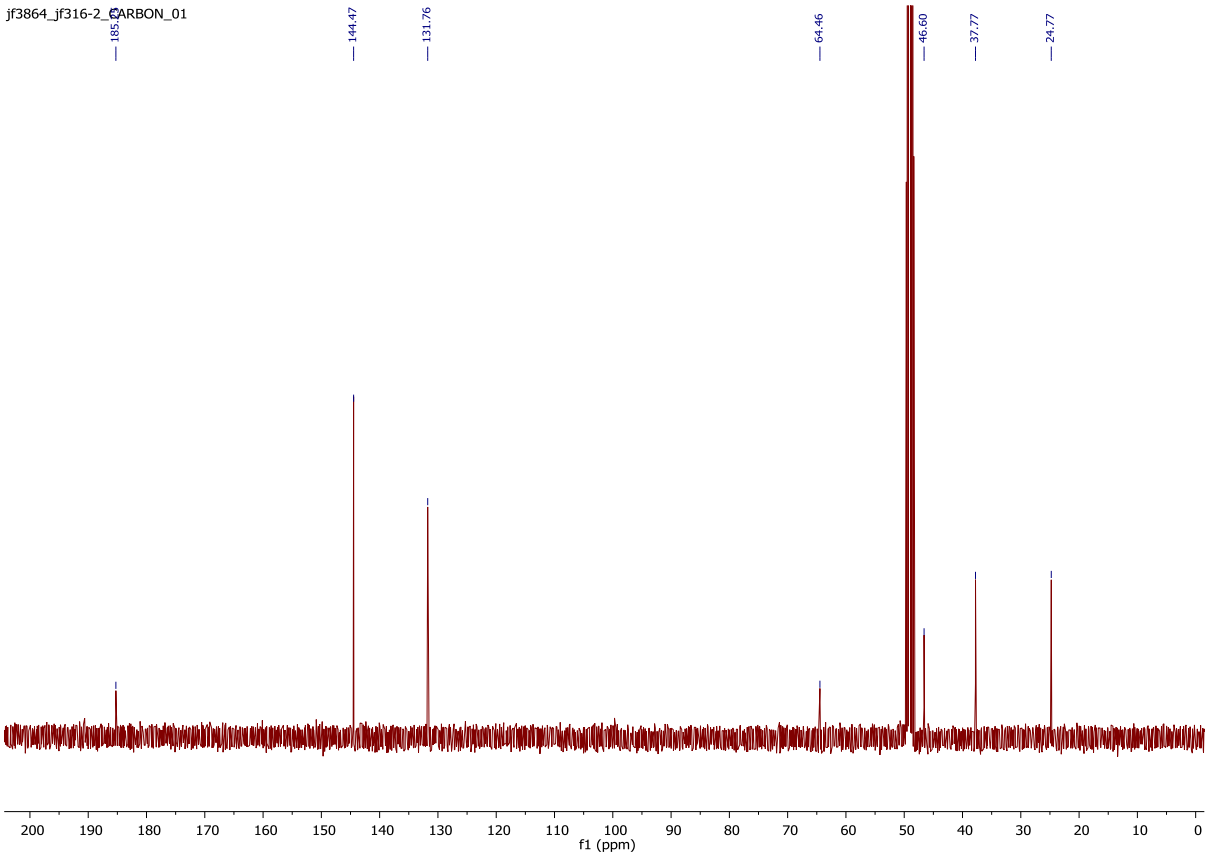
tert-Butyl (3-(4-hydroxyphenyl)propyl)(tosyloxy)carbamate (5a)



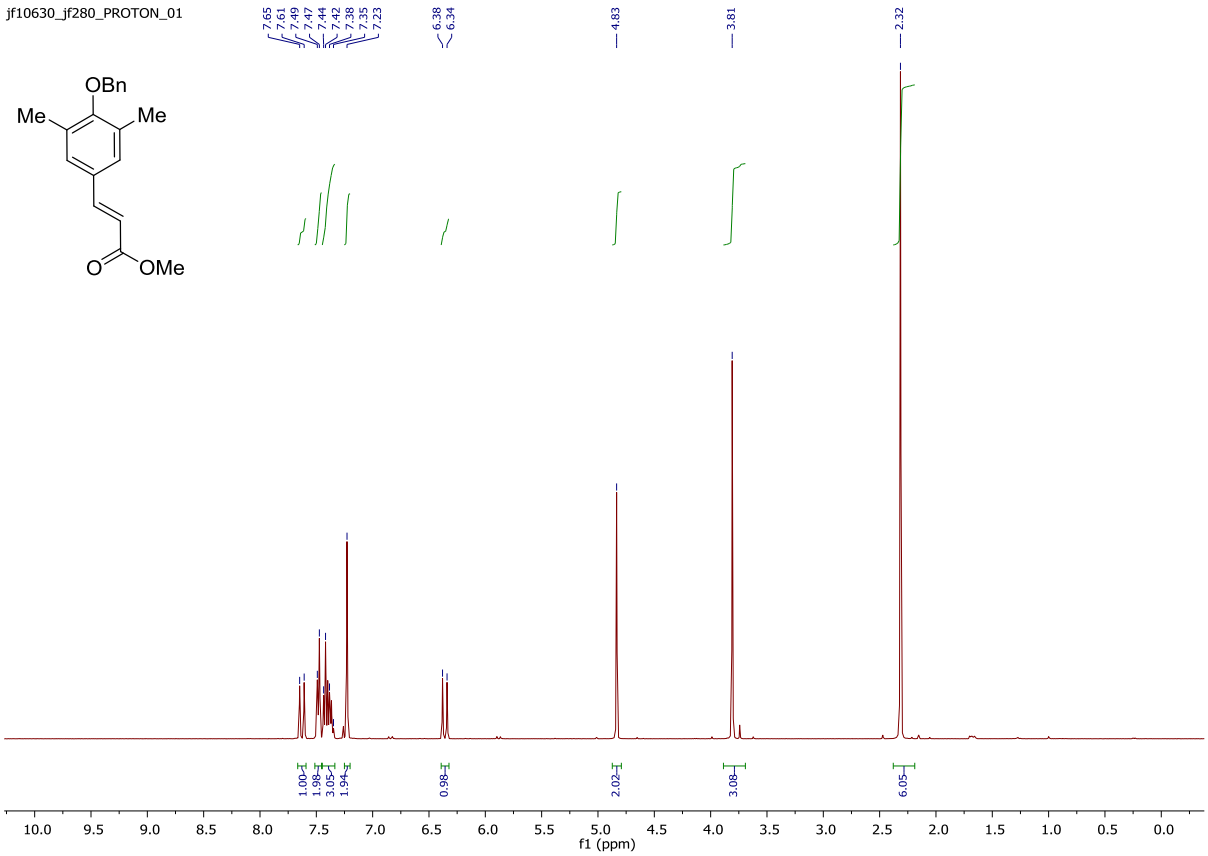


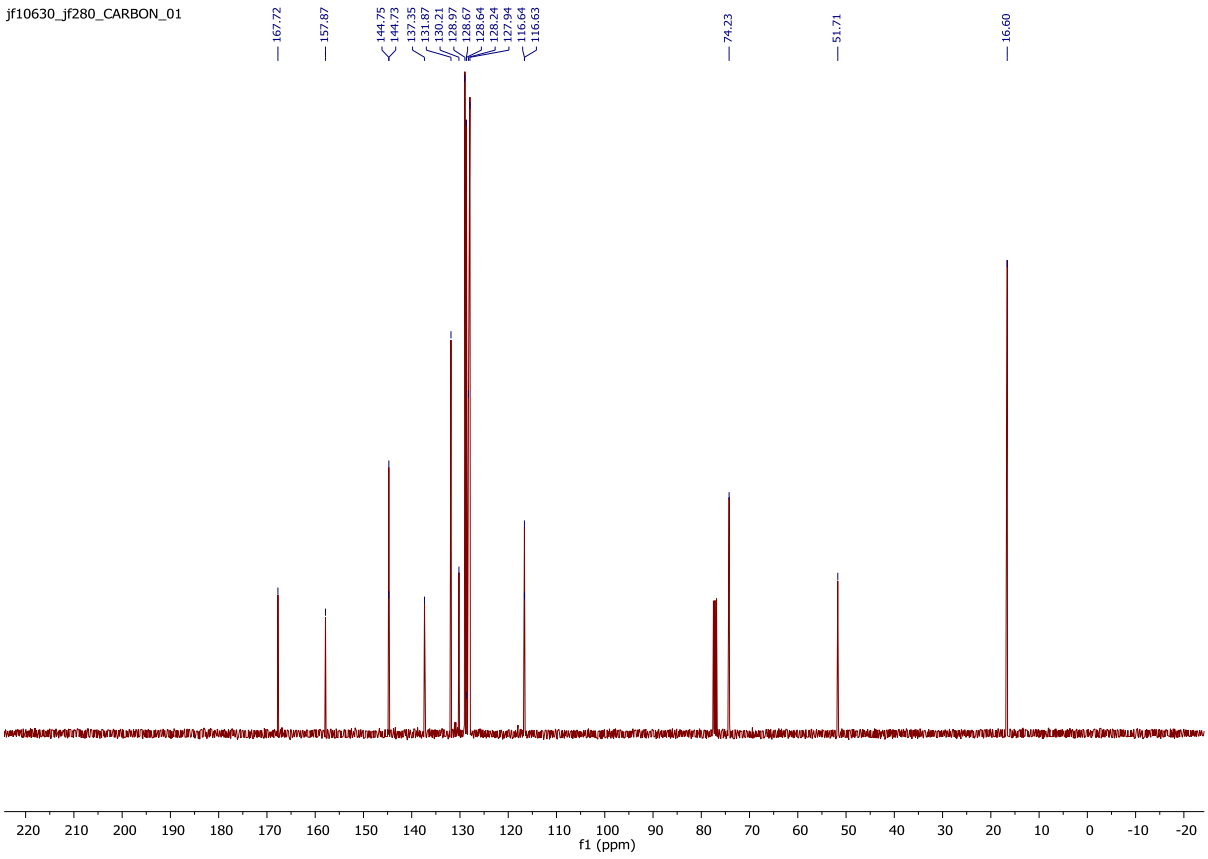
1-Azaspiro[4.5]deca-6,9-dien-8-one trifluoroacetate (7a)



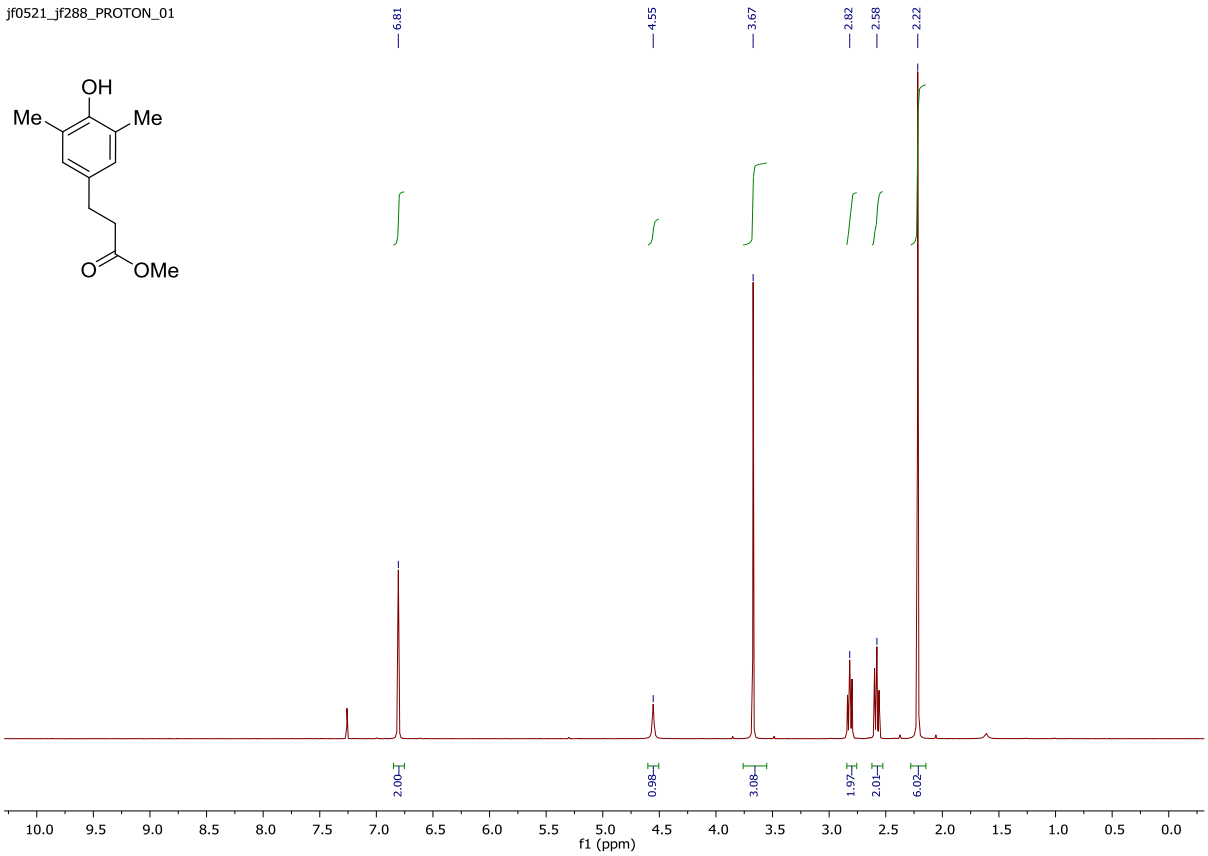


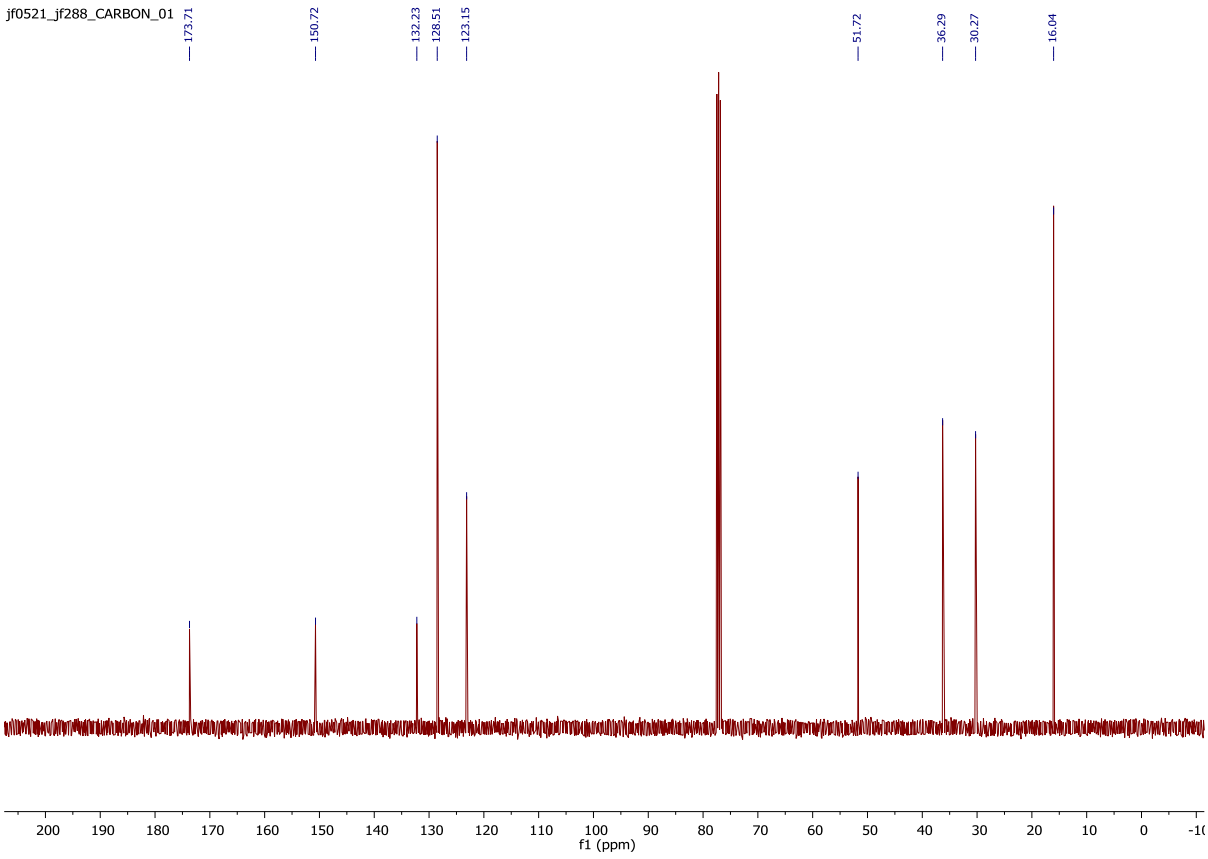
Methyl (*E*)-3-(4-(benzyloxy)-3,5-dimethylphenyl)acrylate



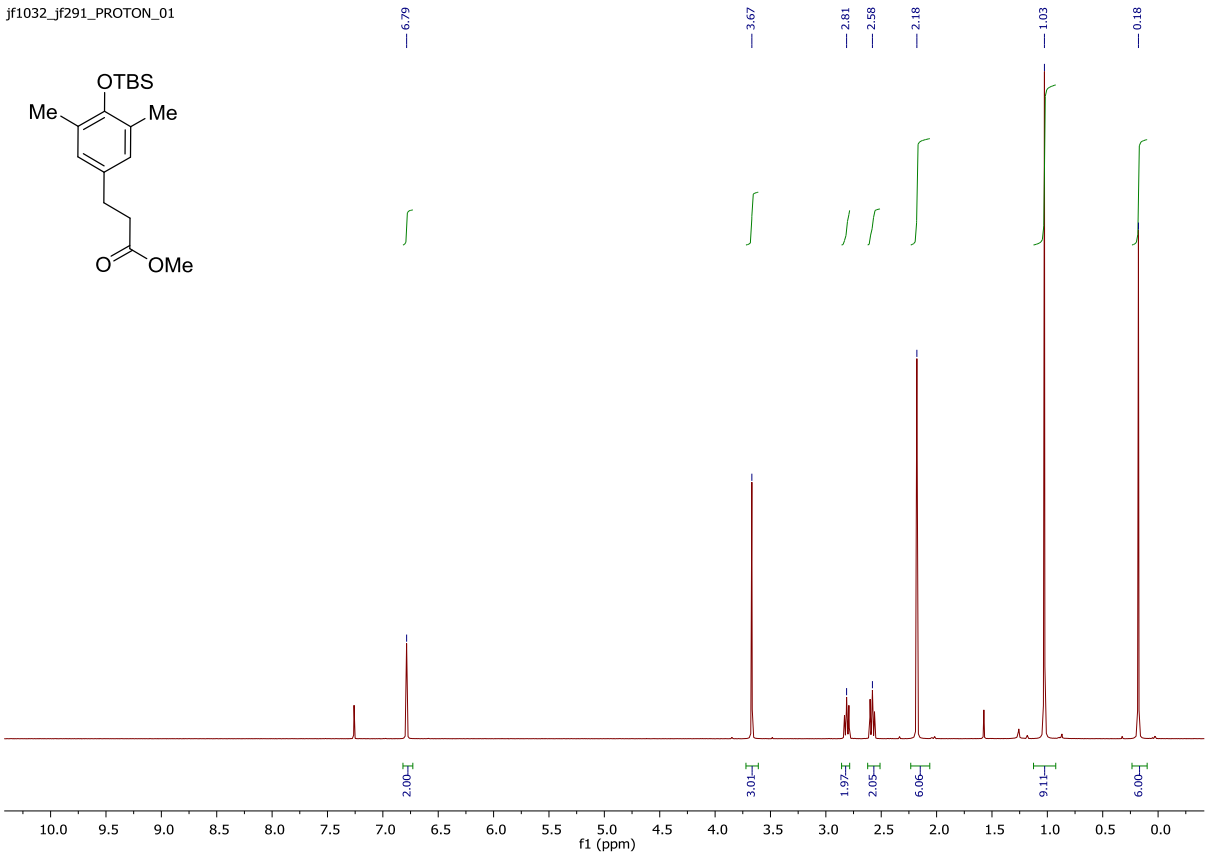


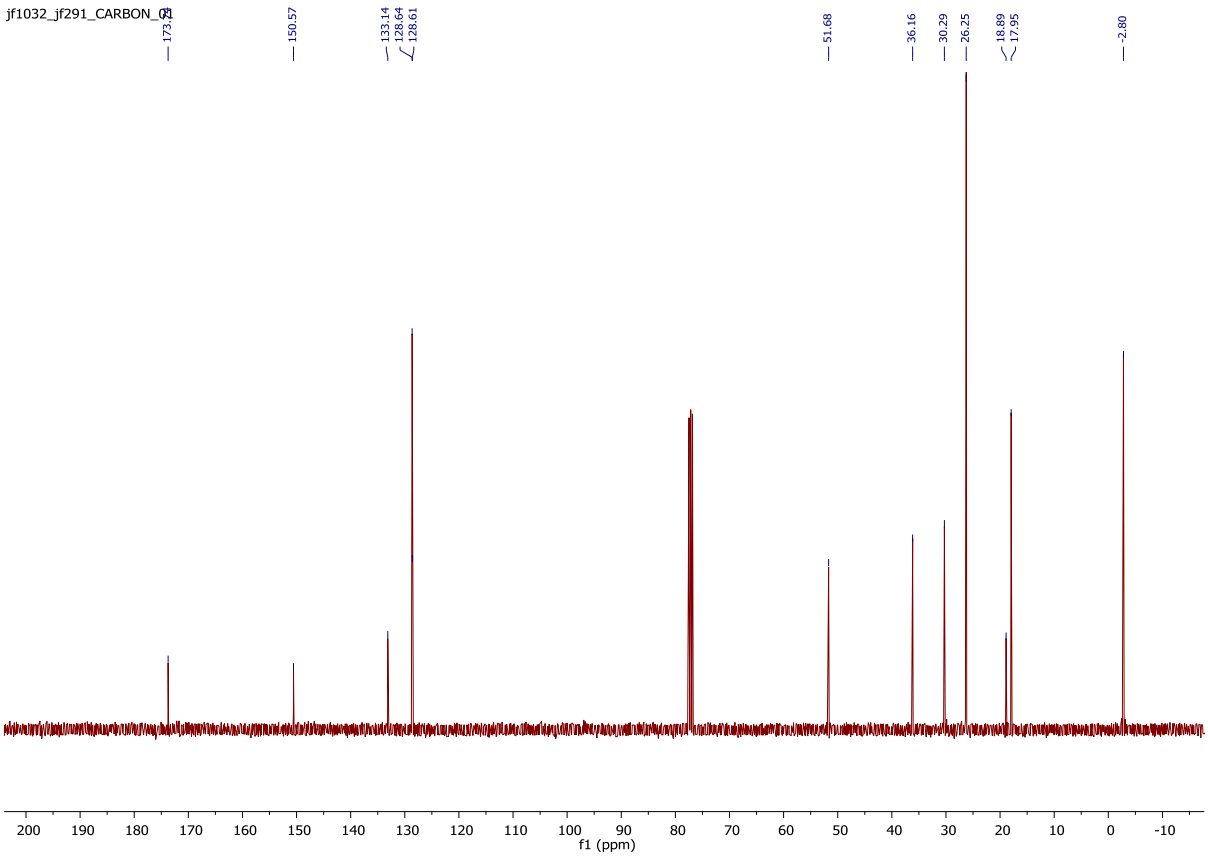
Methyl 3-(4-hydroxy-3,5-dimethylphenyl)propanoate



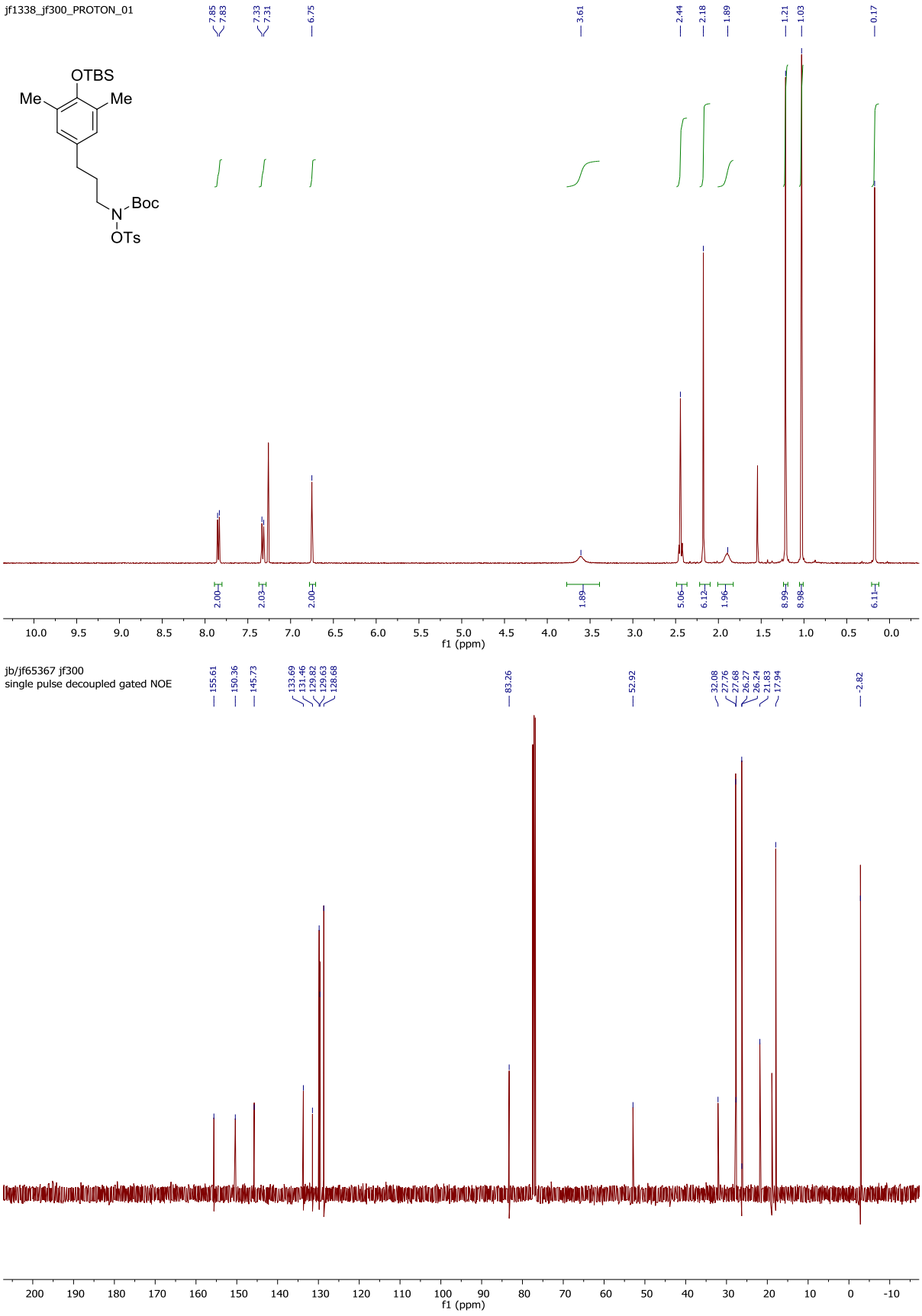


Methyl 3-(4-((*tert*-butyldimethylsilyl)oxy)-3,5-dimethylphenyl)propanoate

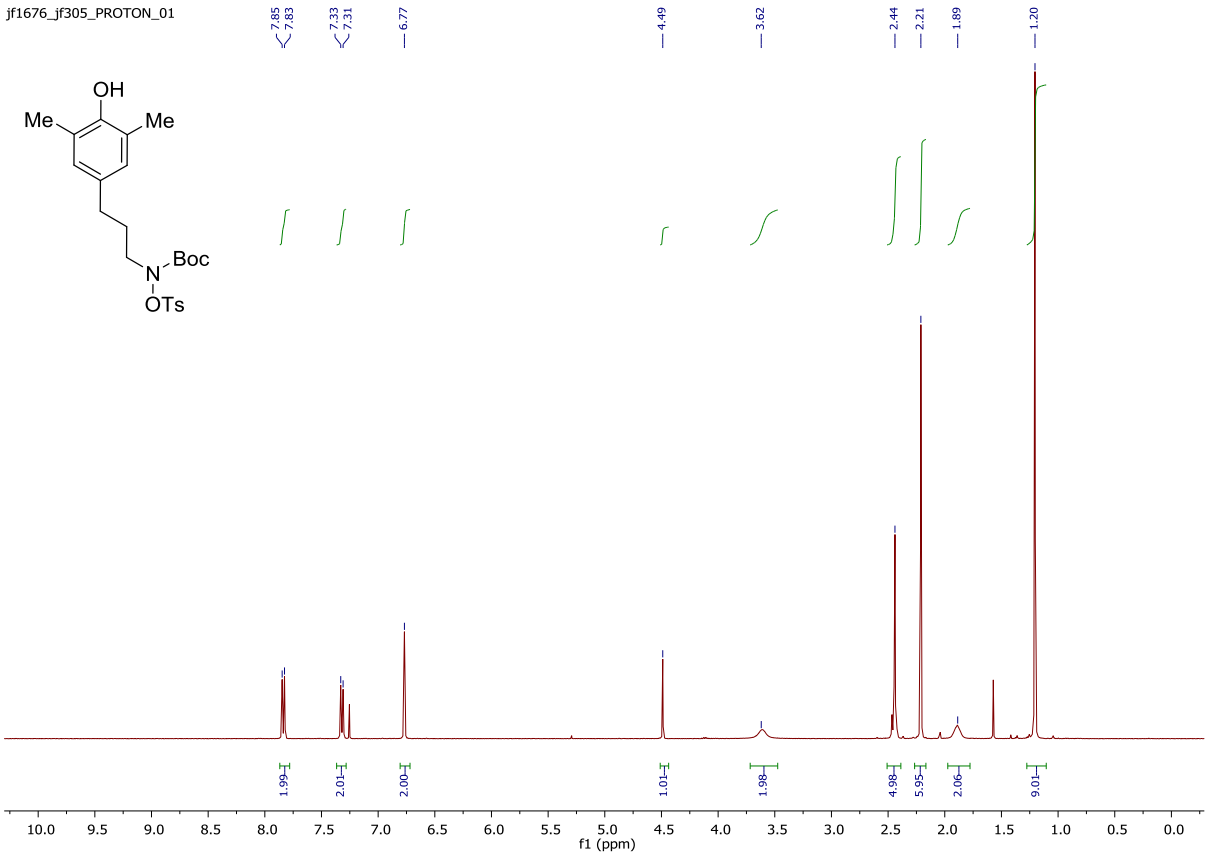


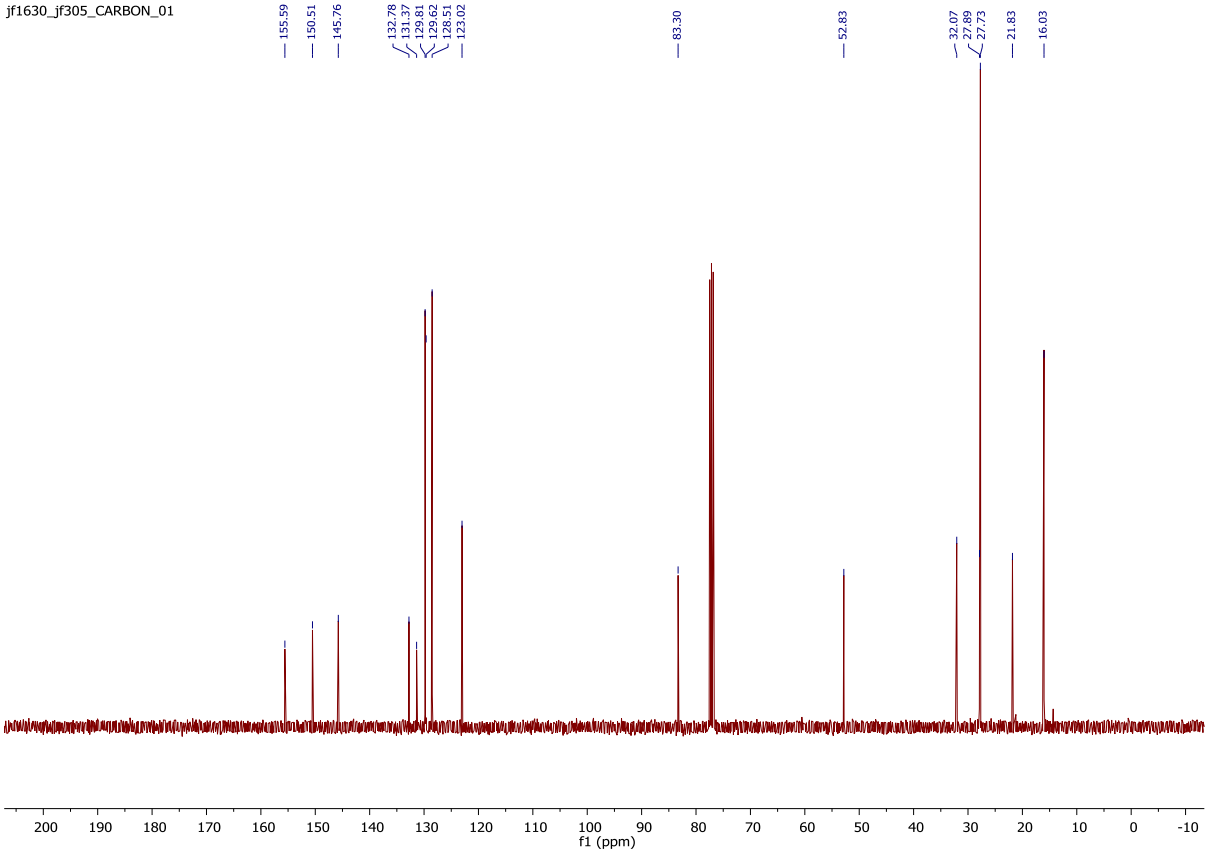


tert-Butyl(3-(4-((*tert*-butyldimethylsilyl)oxy)-3,5-dimethylphenyl)propyl)(tosyloxy) carbamate

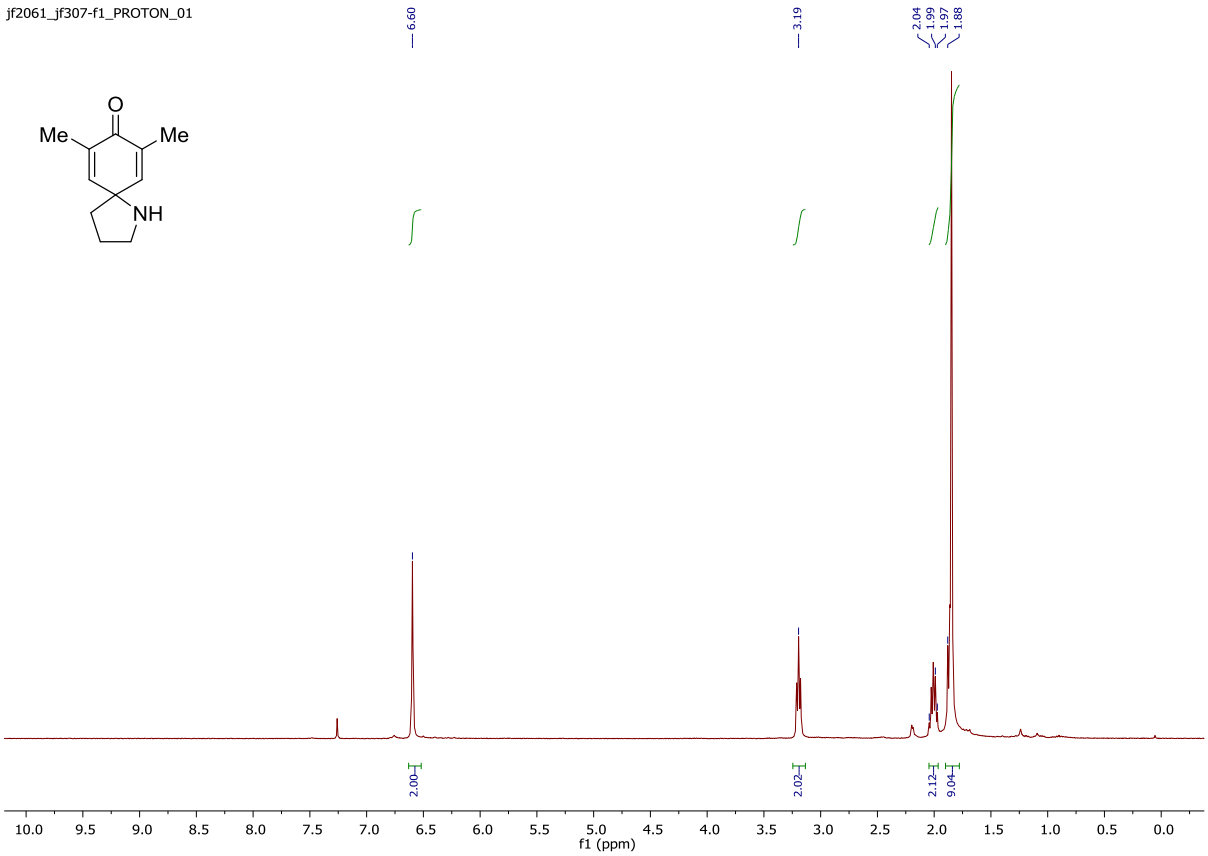


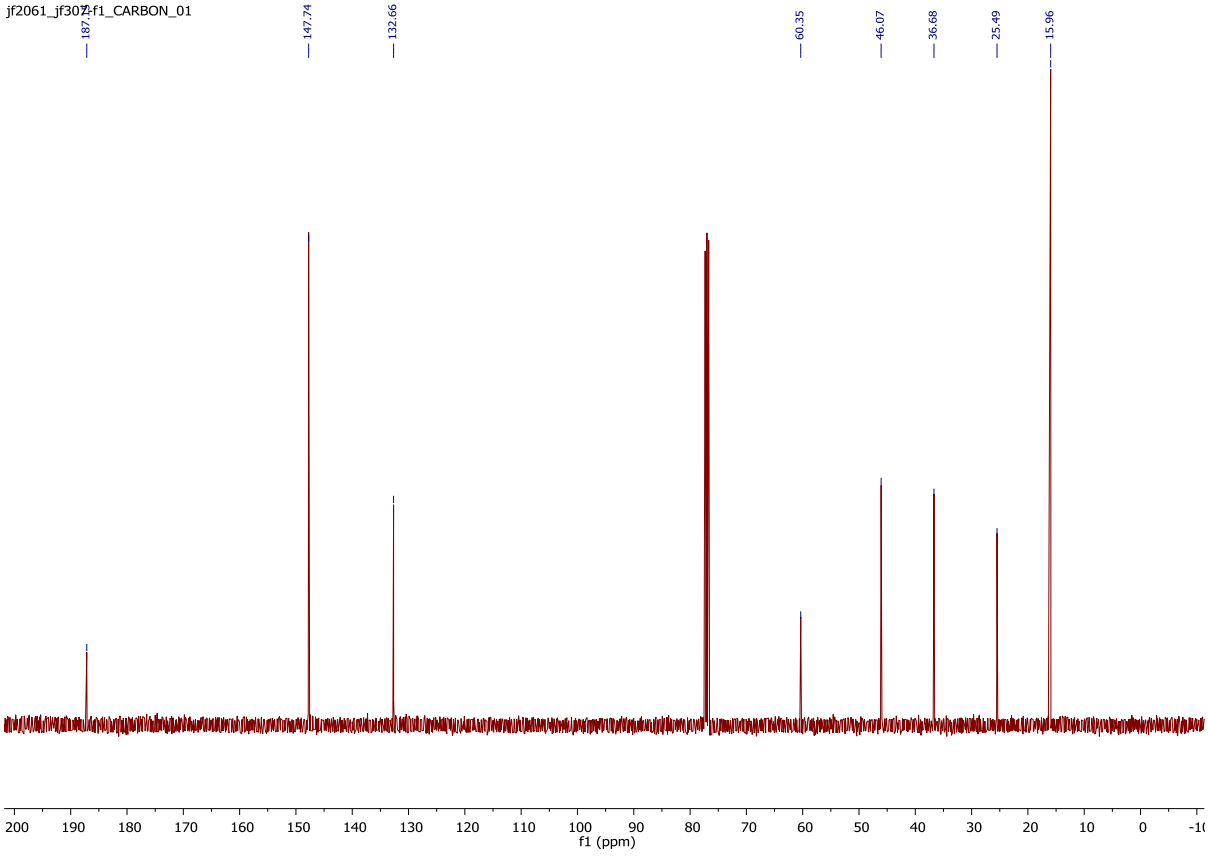
tert-Butyl (3-(4-hydroxy-3,5-dimethylphenyl)propyl)(tosyloxy)carbamate (5b)



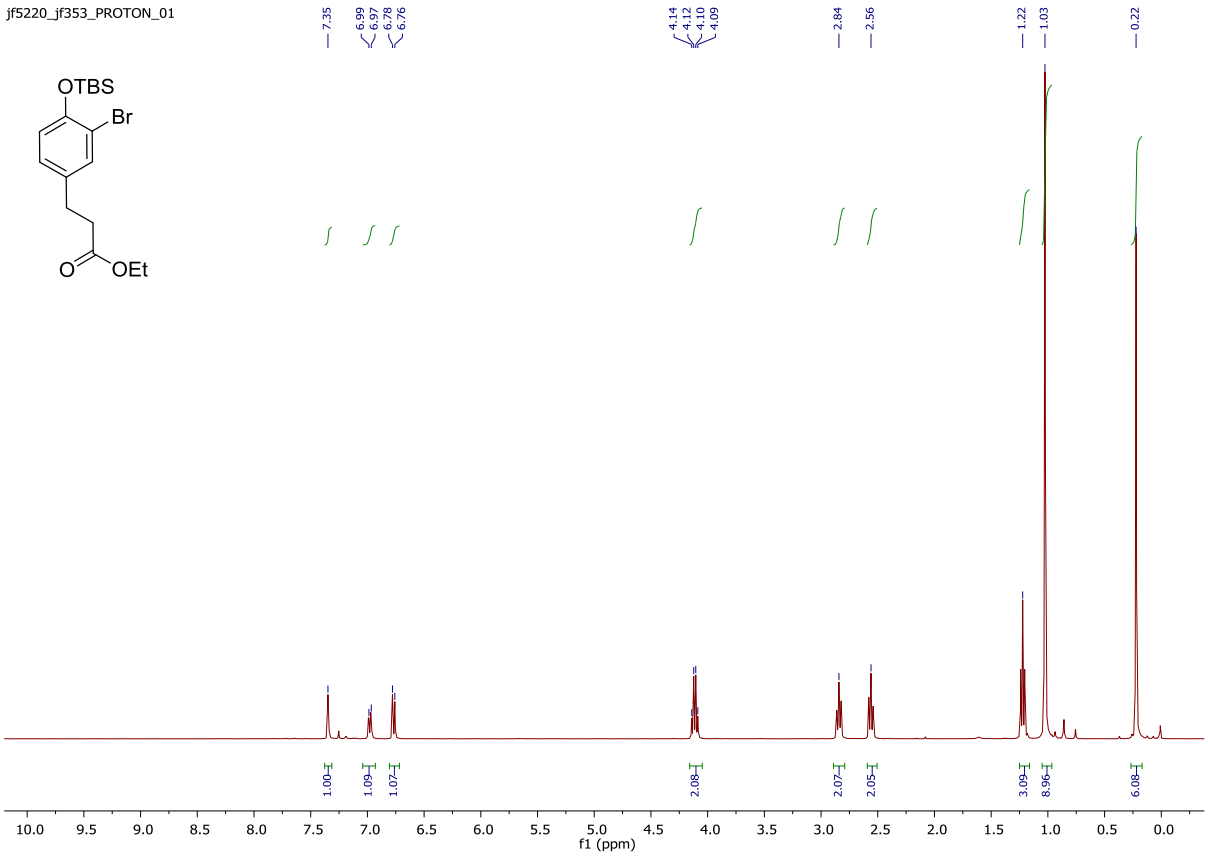


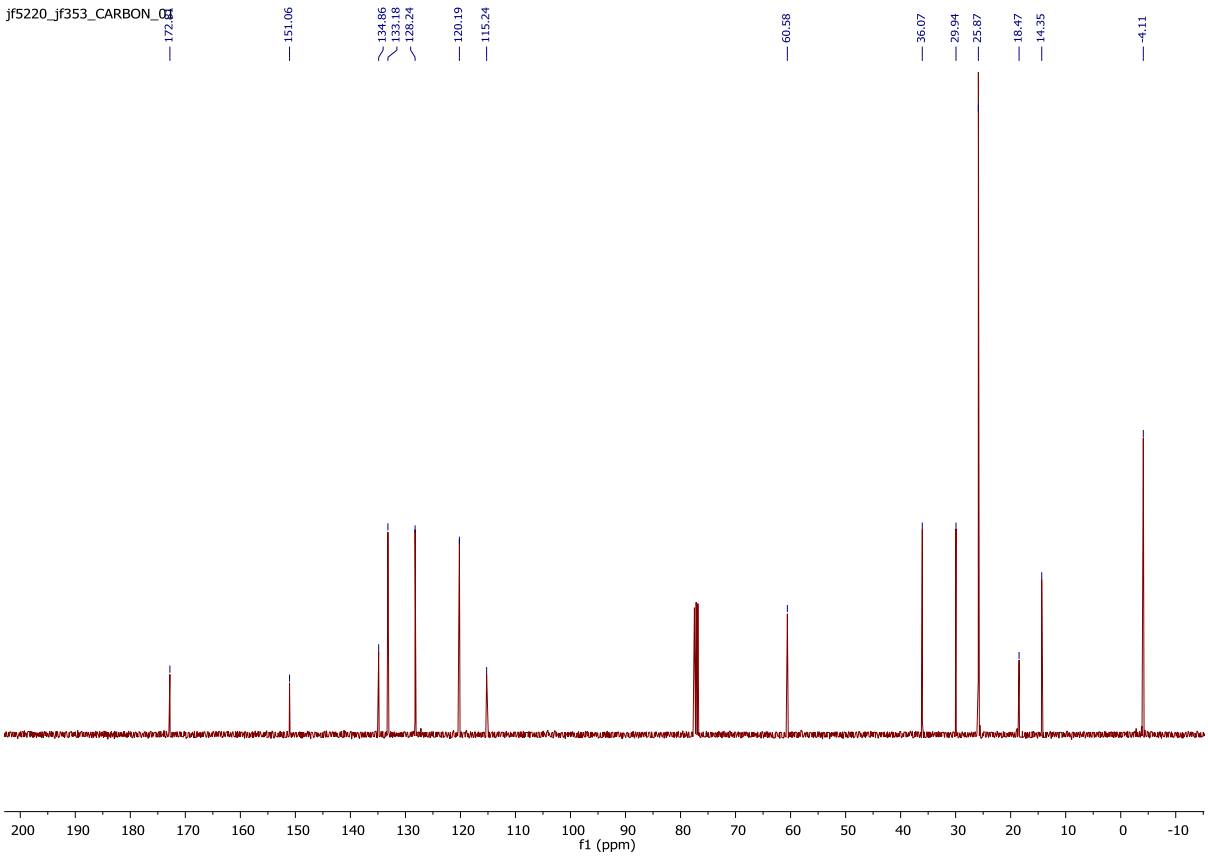
7,9-Dimethyl-1-azaspiro[4.5]deca-6,9-dien-8-one (7b)



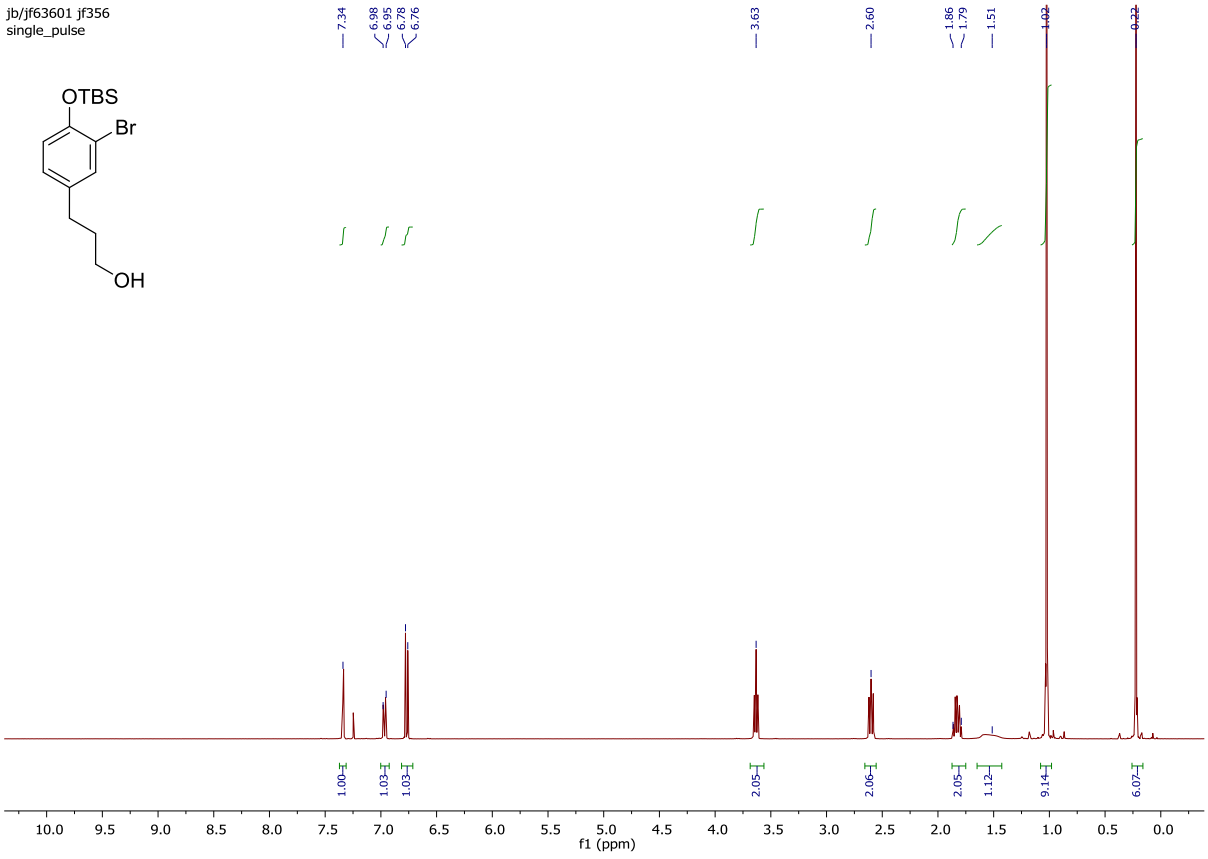


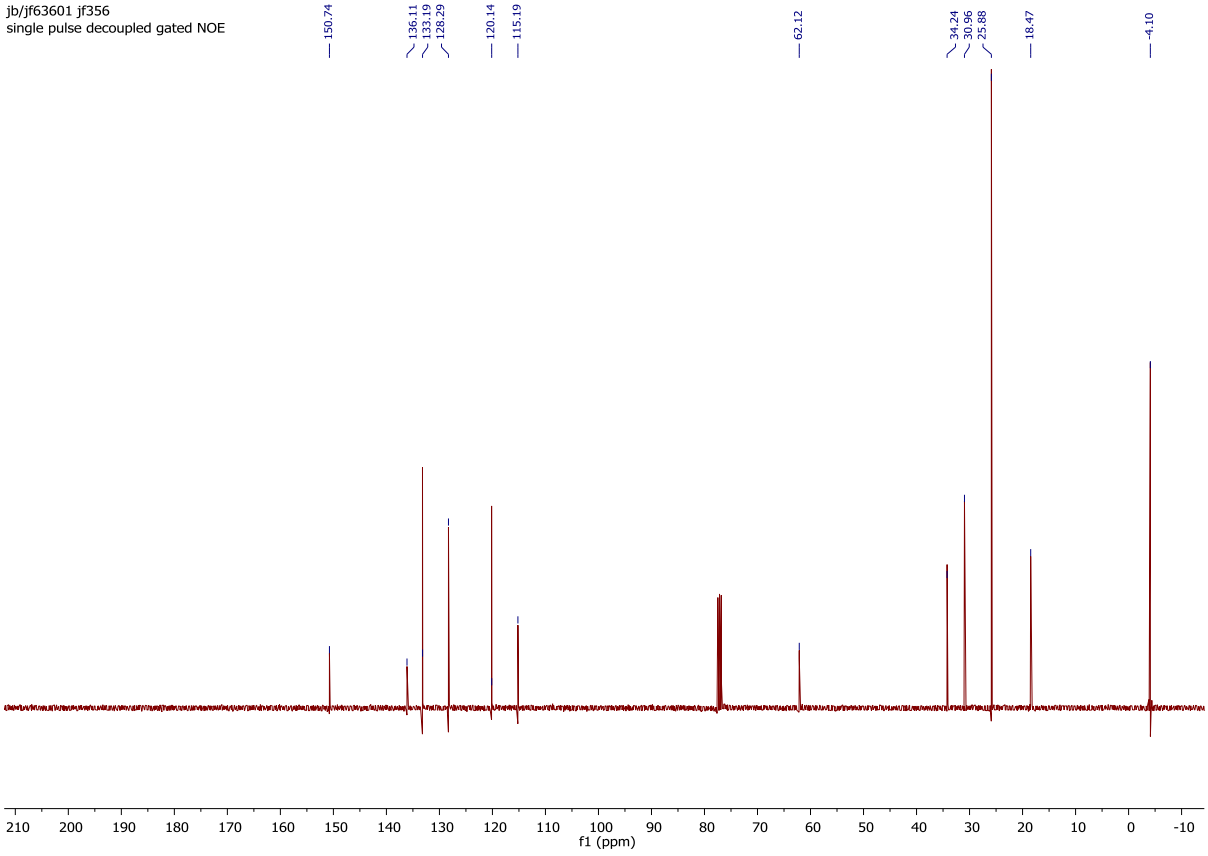
Ethyl 3-(3-bromo-4-((*tert*-butyldimethylsilyl)oxy)phenyl)propanoate



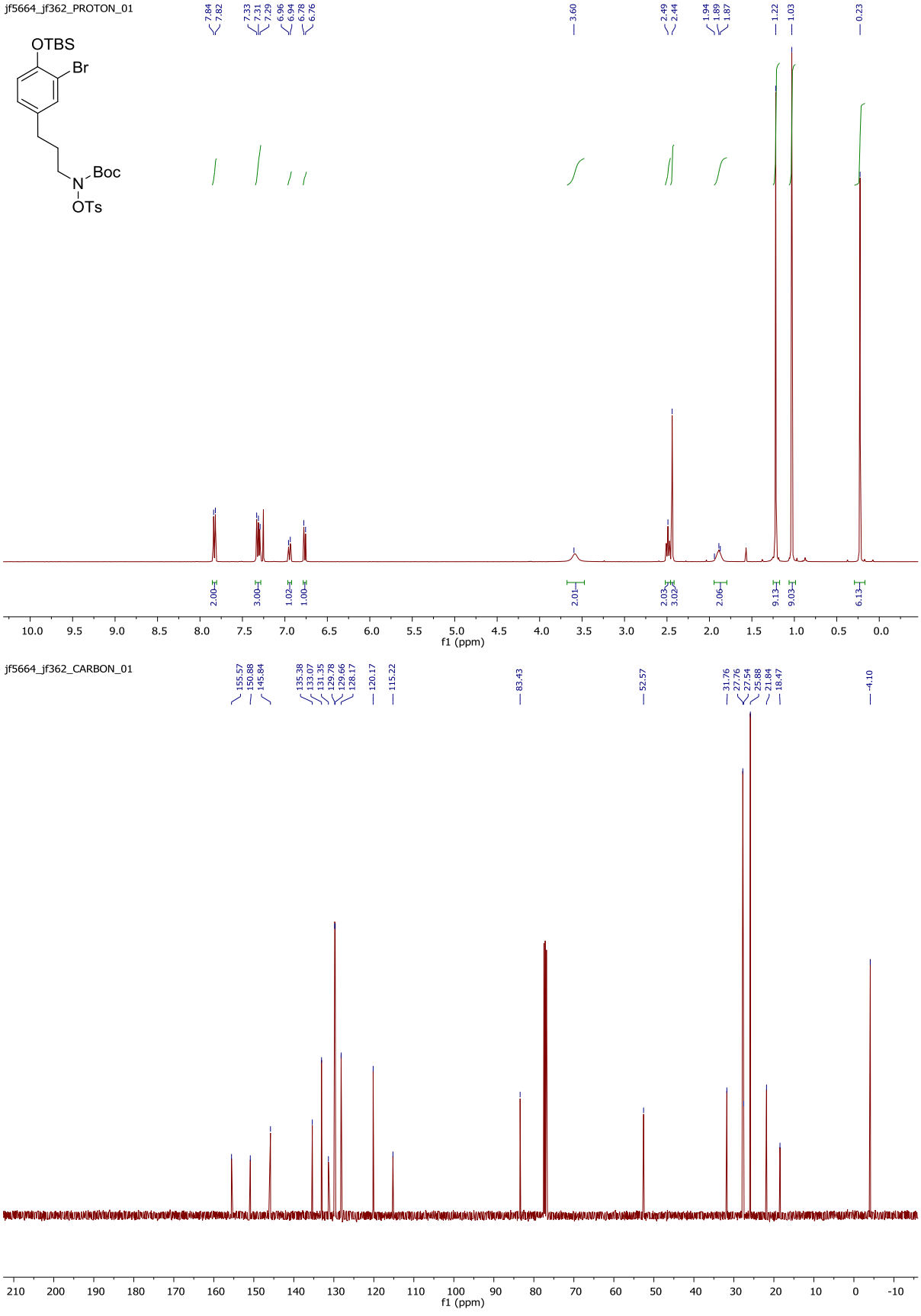


3-(3-Bromo-4-((*tert*-butyldimethylsilyl)oxy)phenyl)propan-1-ol

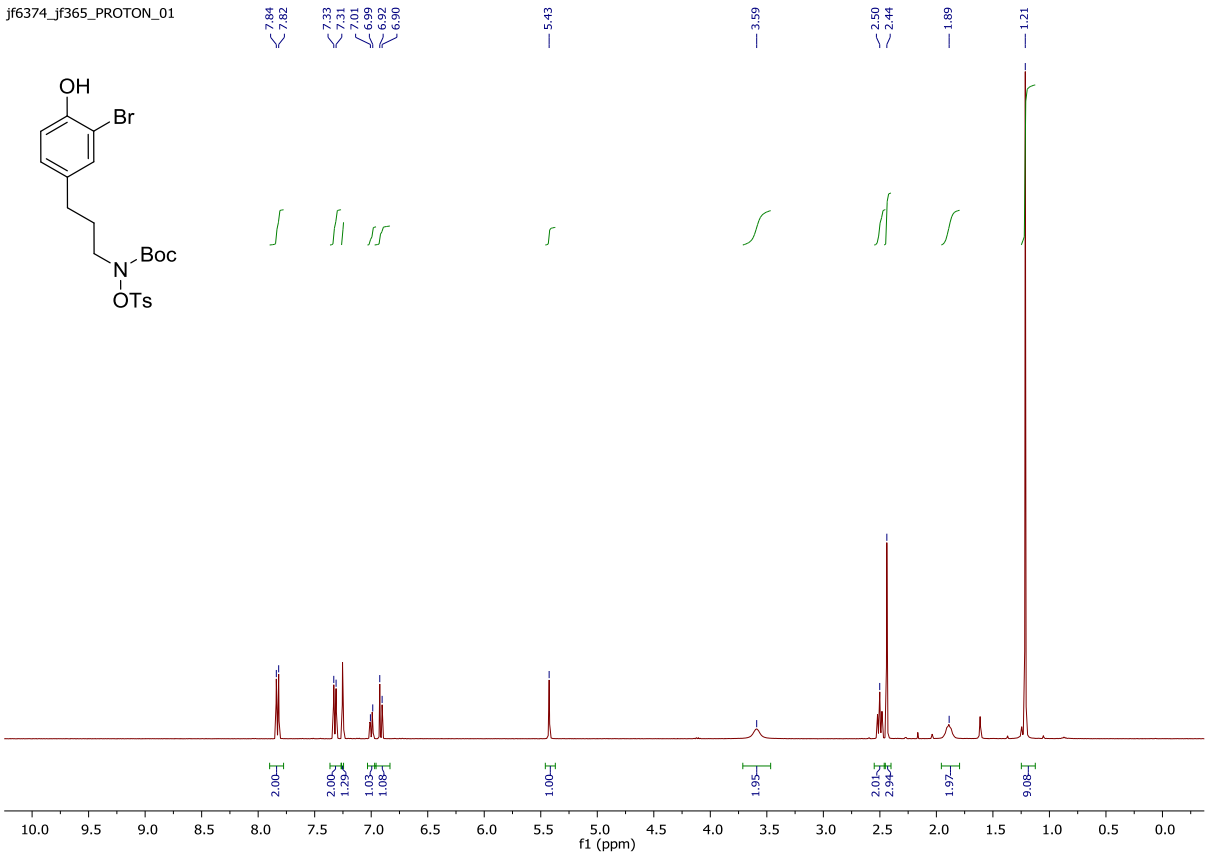


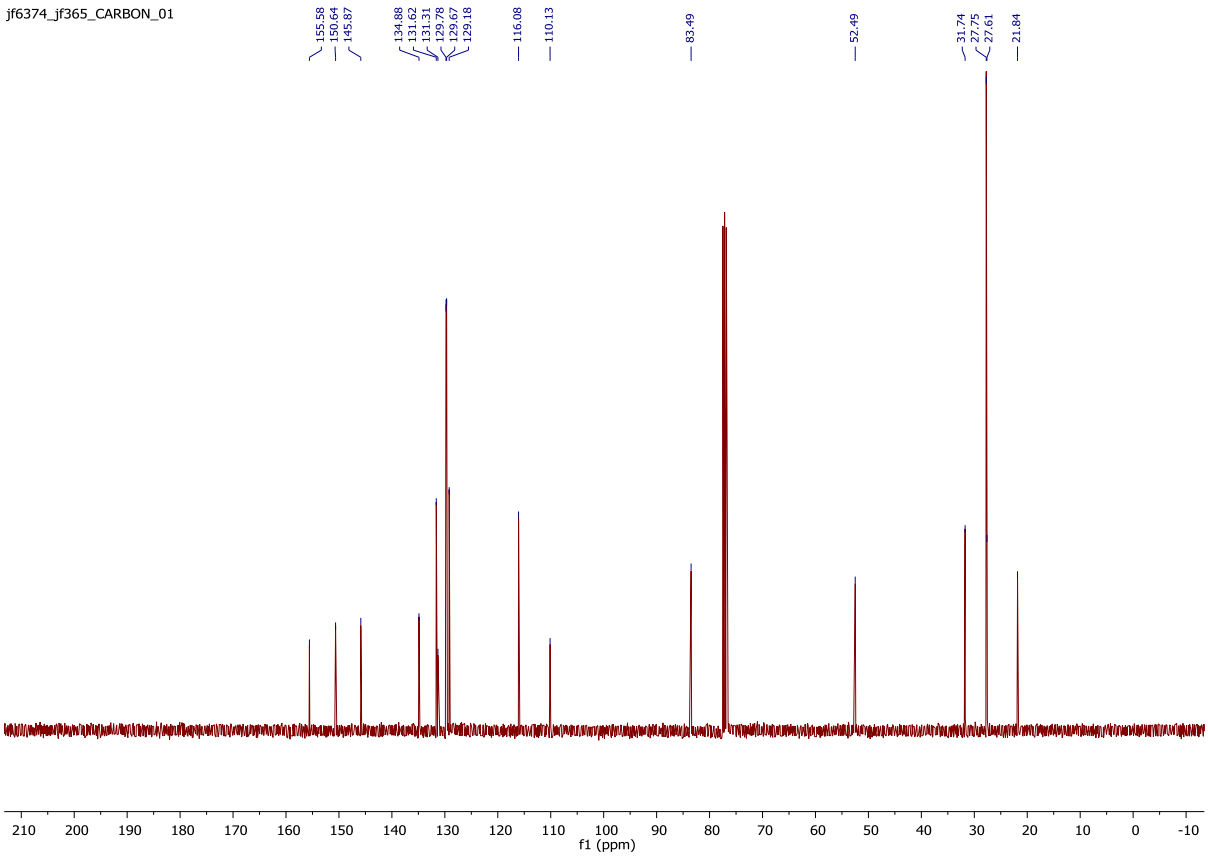


tert-Butyl(3-(3-bromo-4-((_tert_-butyldimethylsilyl)oxy)phenyl)propyl)(tosyloxy) carbamate

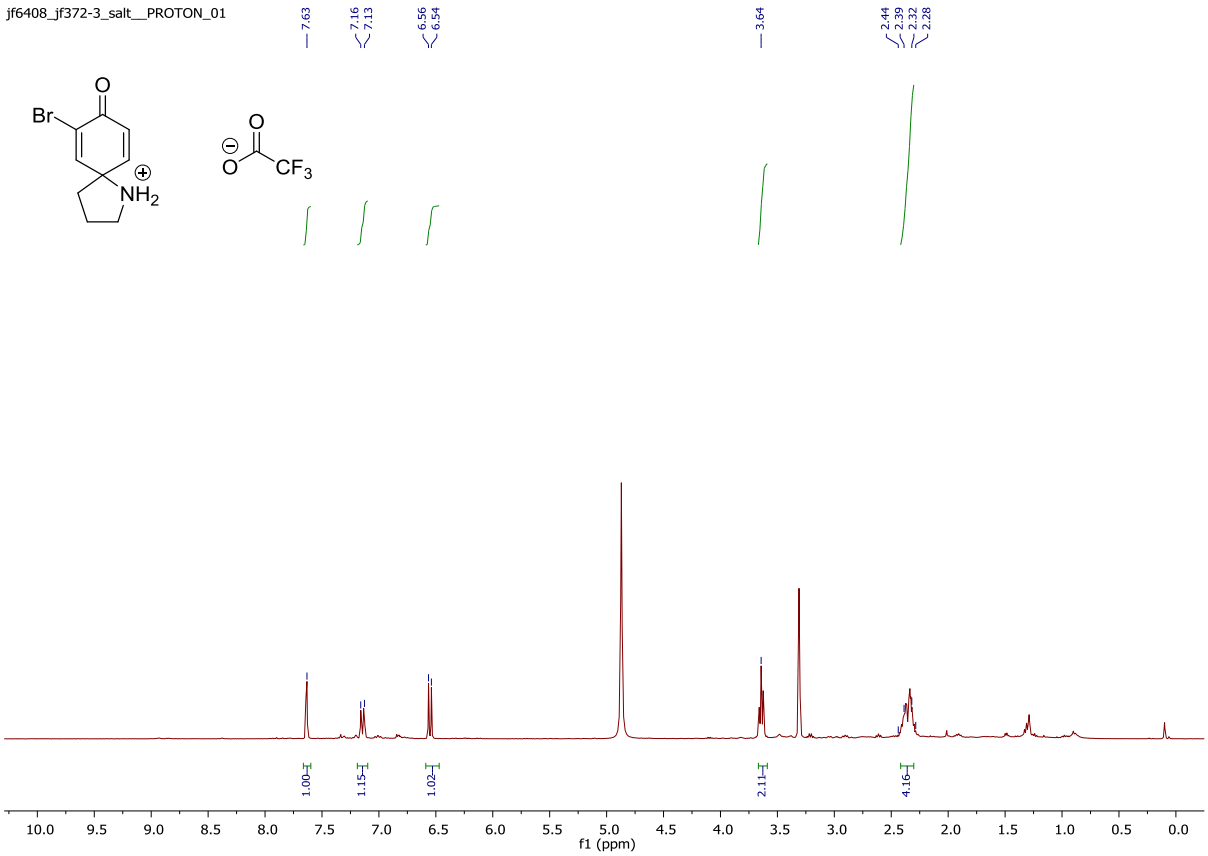


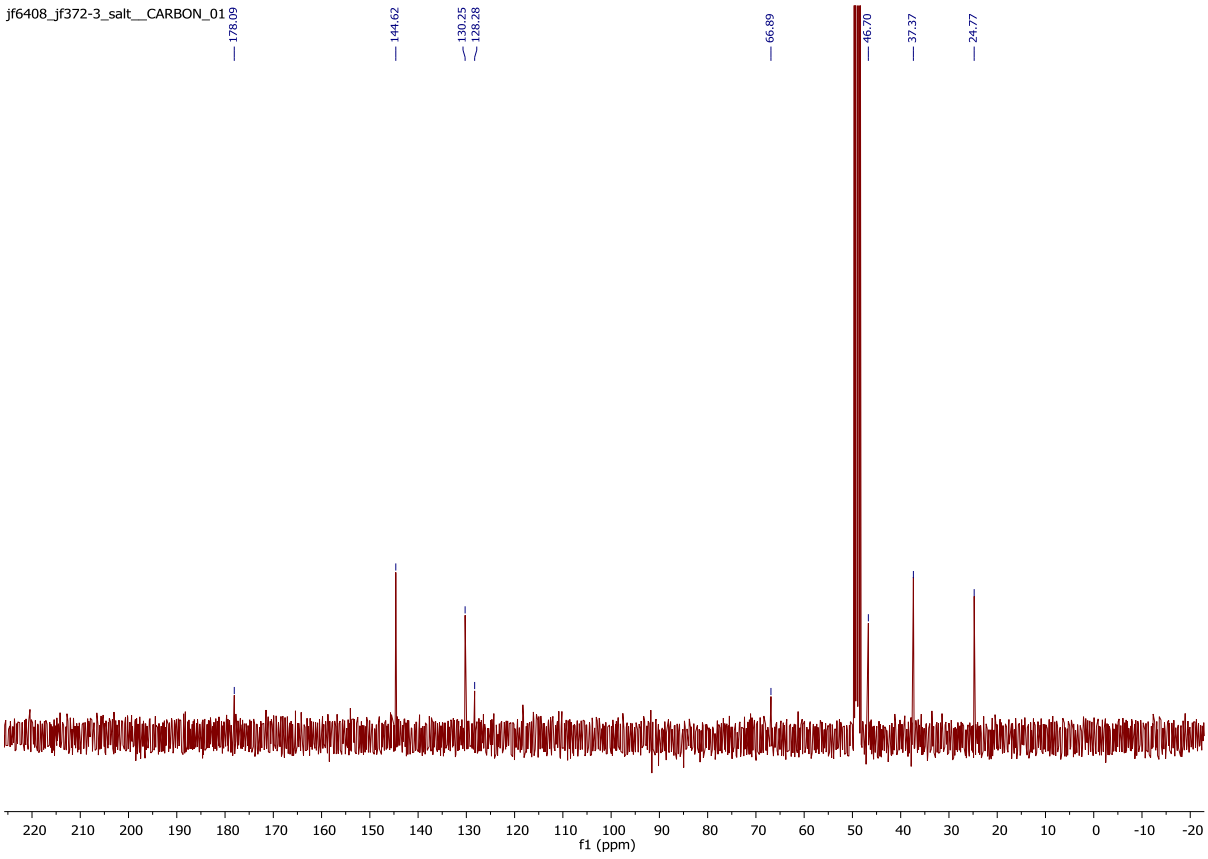
tert-Butyl (3-(3-bromo-4-hydroxyphenyl)propyl)(tosyloxy)carbamate (5c)



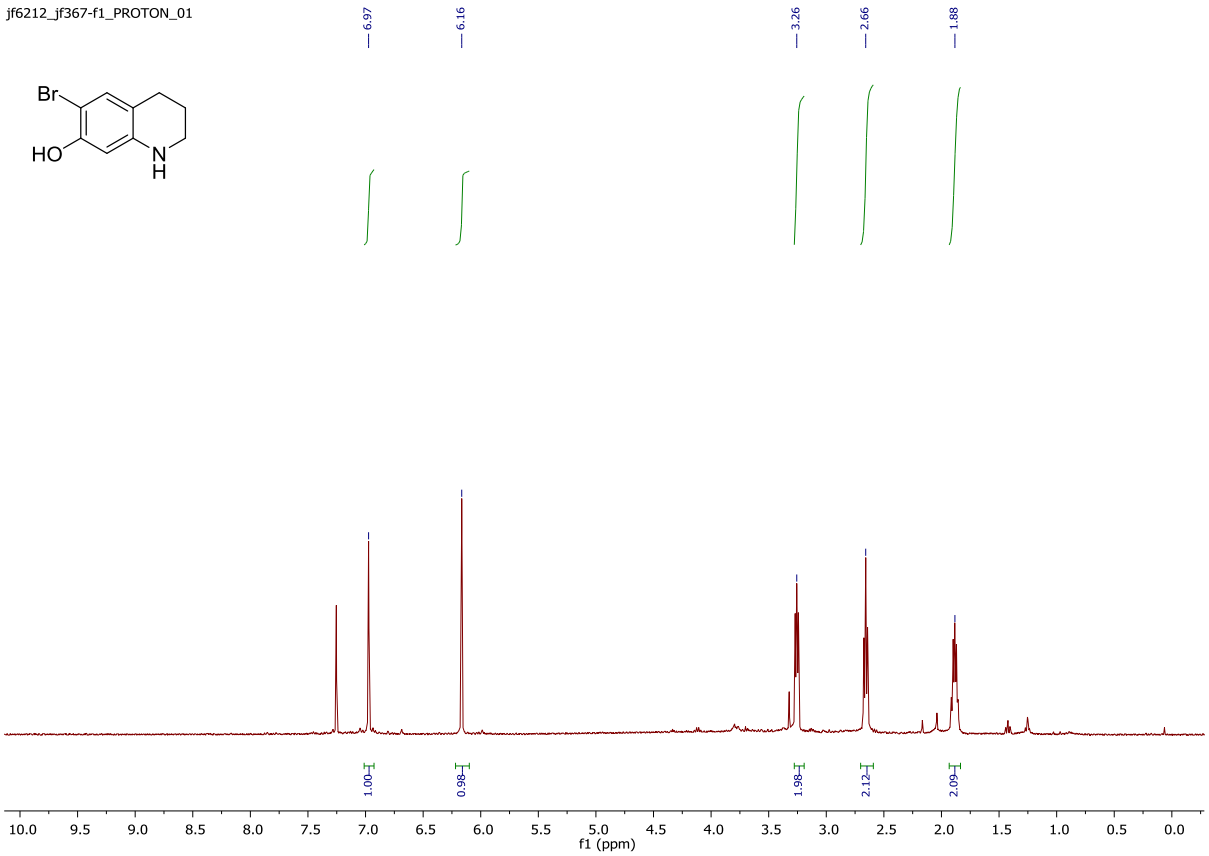


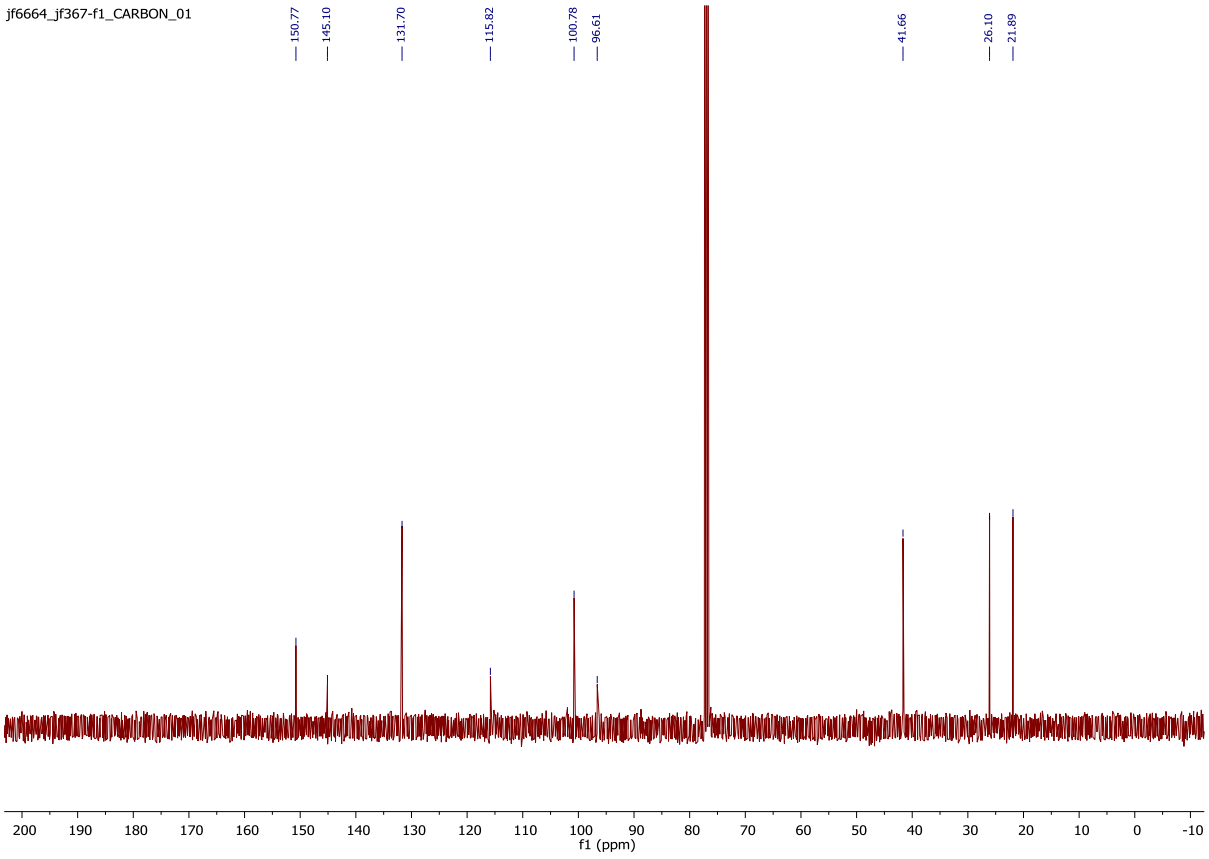
7-Bromo-1-azaspiro[4.5]deca-6,9-dien-8-one trifluoroacetate (7c)



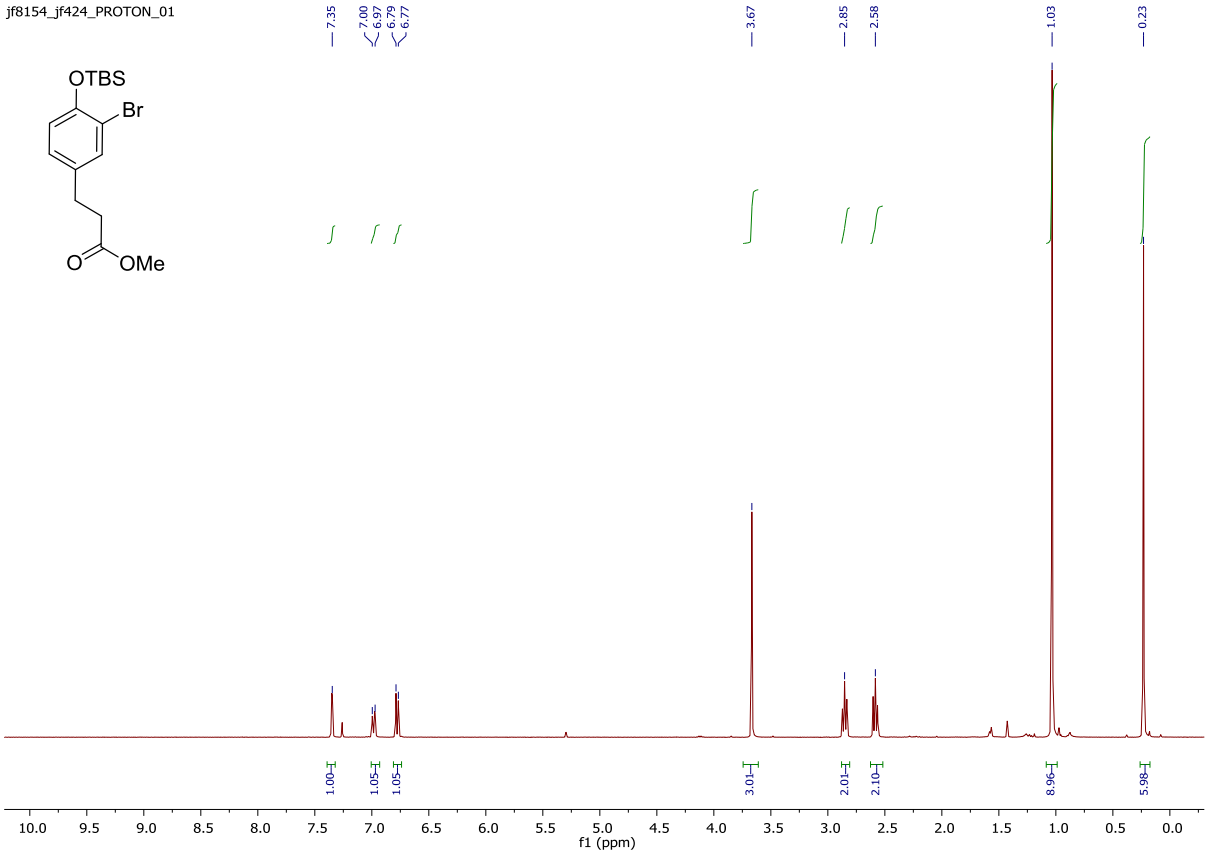


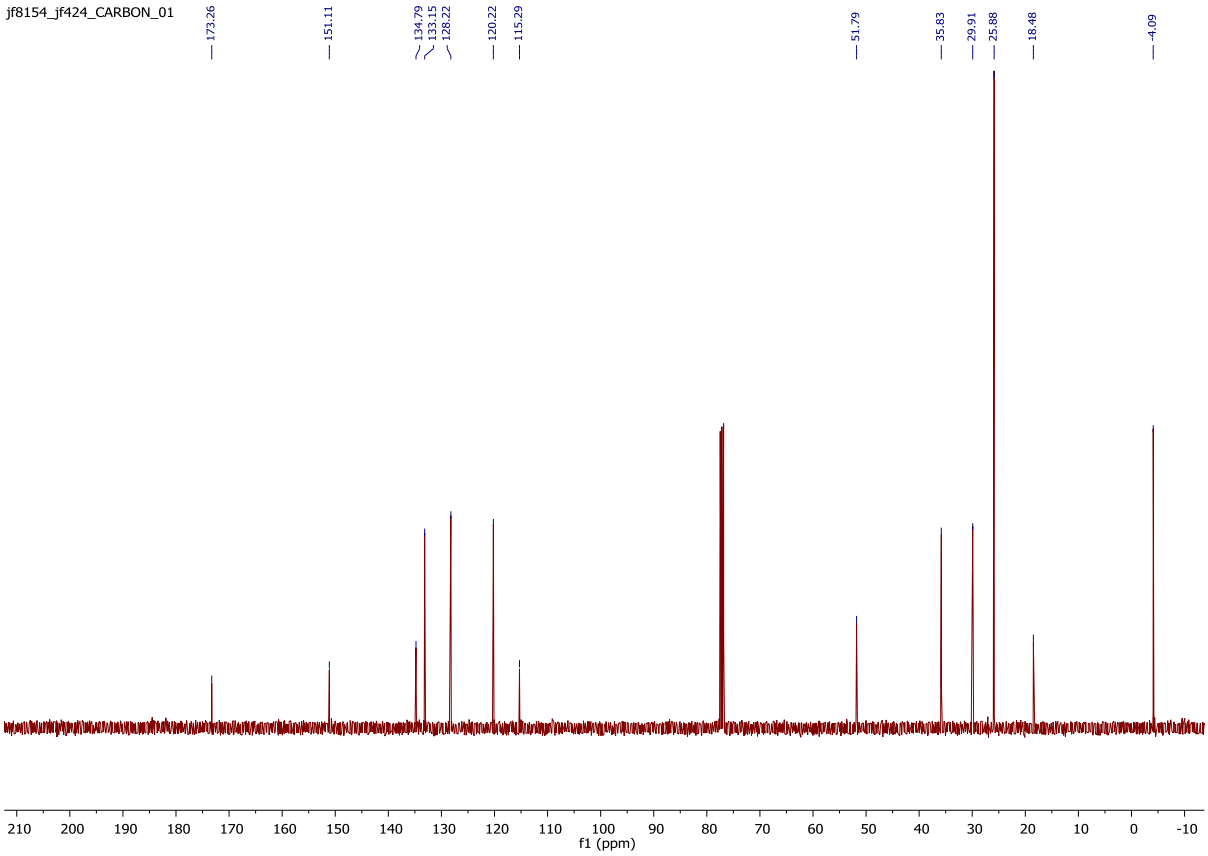
6-Bromo-1,2,3,4-tetrahydroquinolin-7-ol (8c)



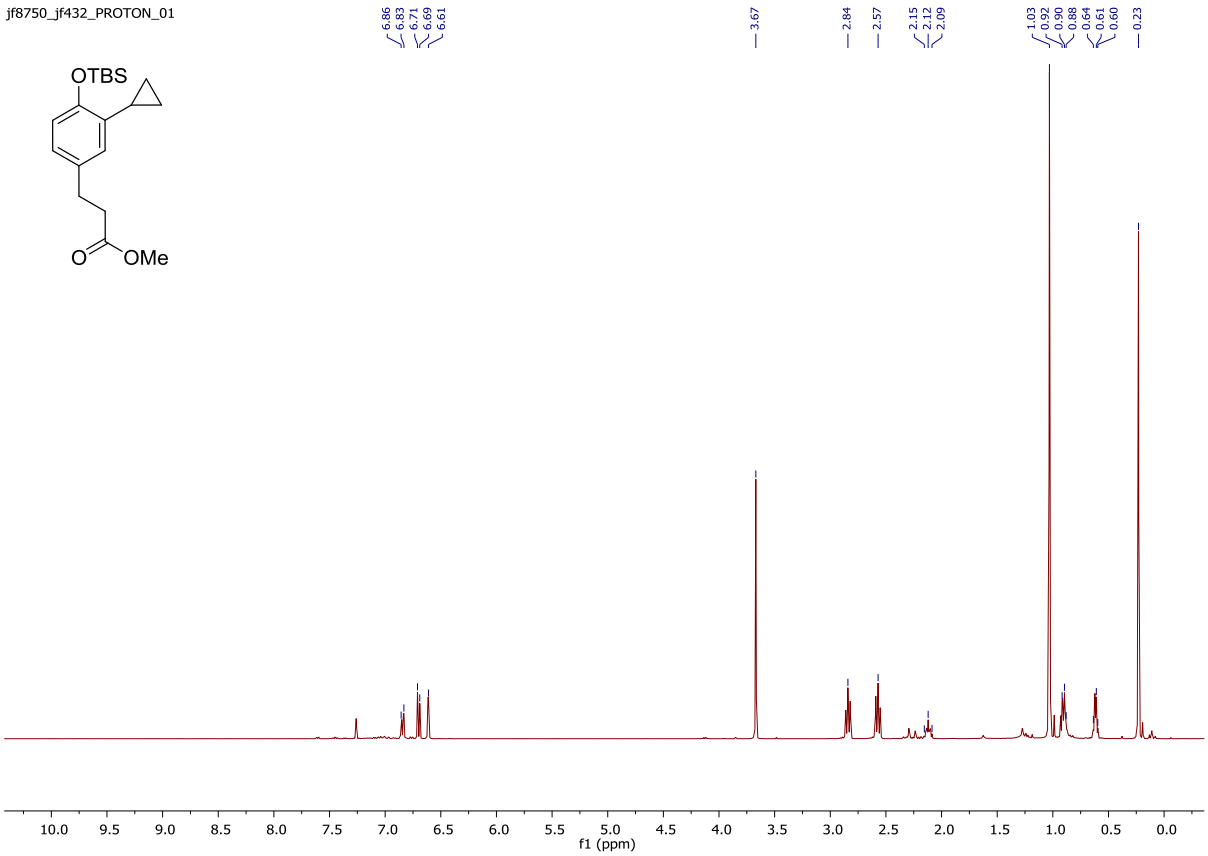


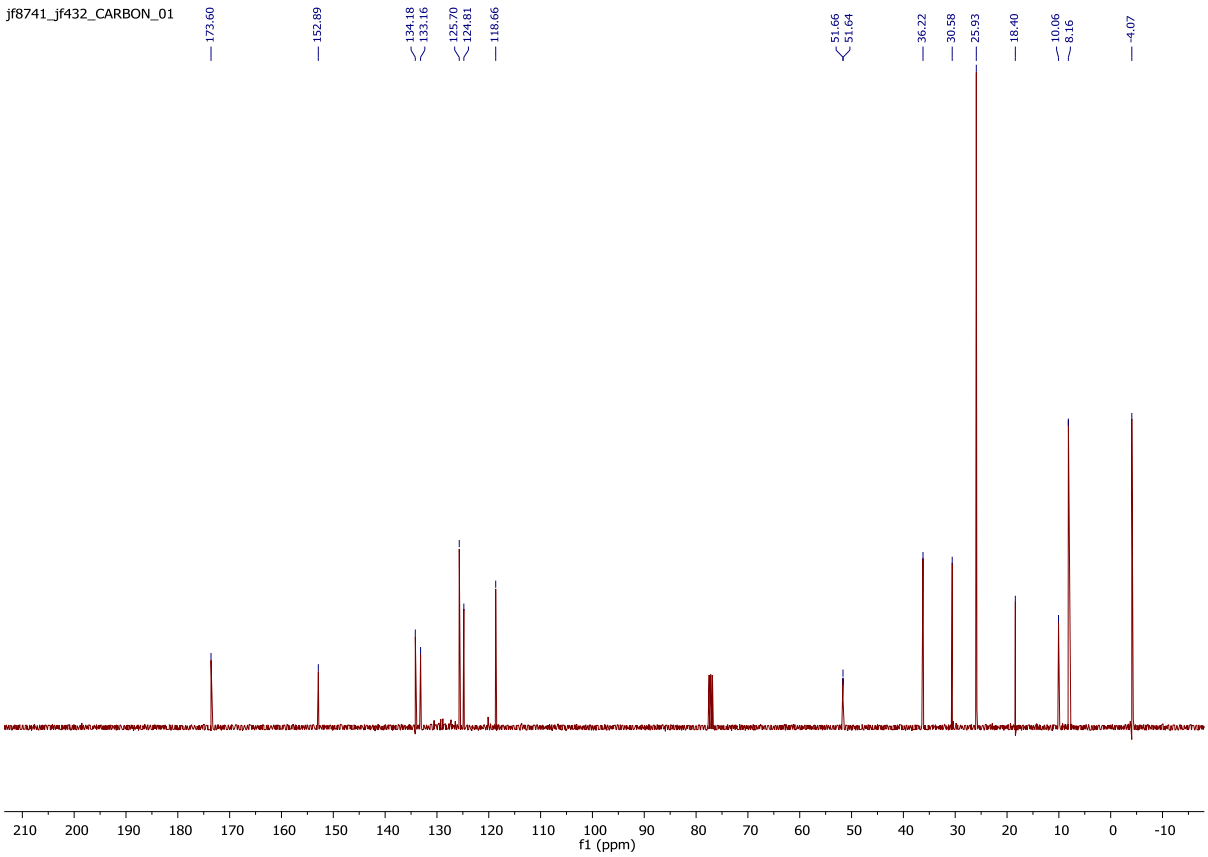
Methyl 3-(3-bromo-4-((*tert*-butyldimethylsilyl)oxy)phenyl)propanoate



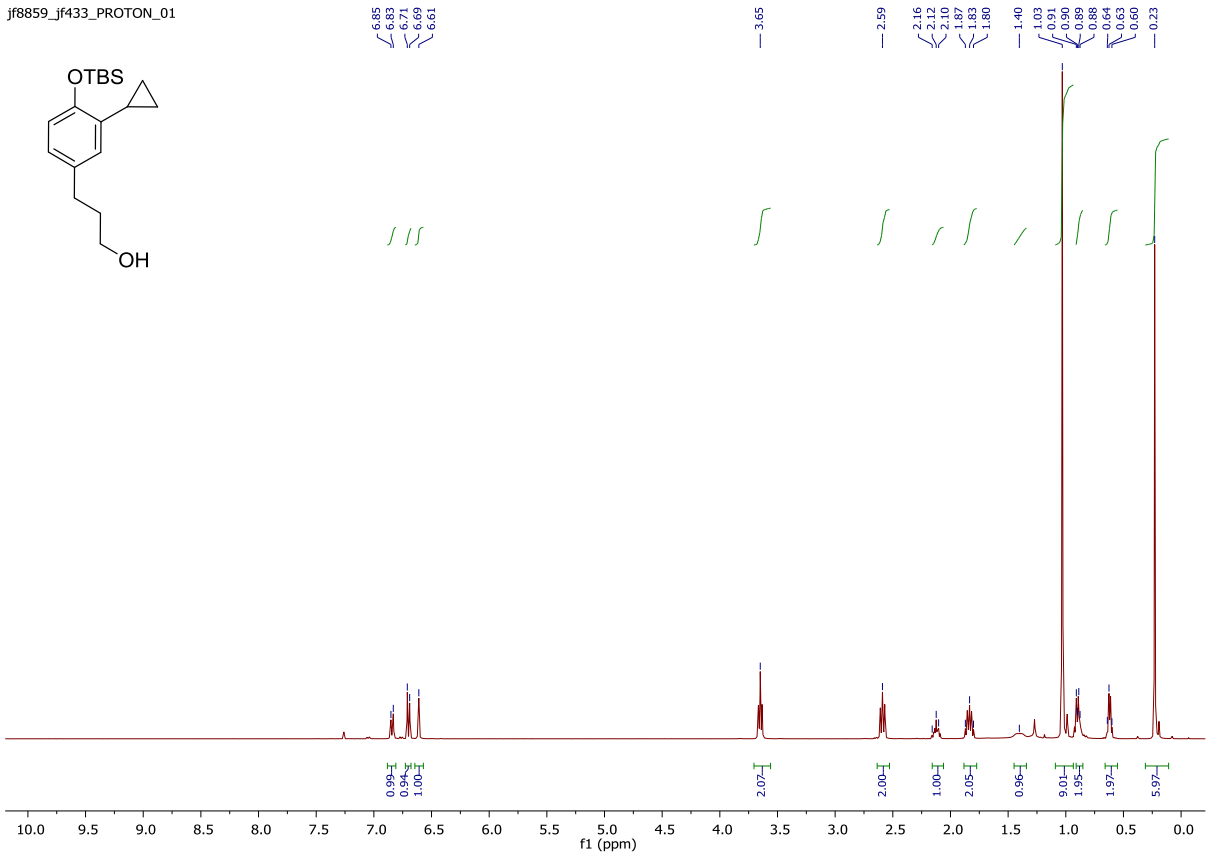


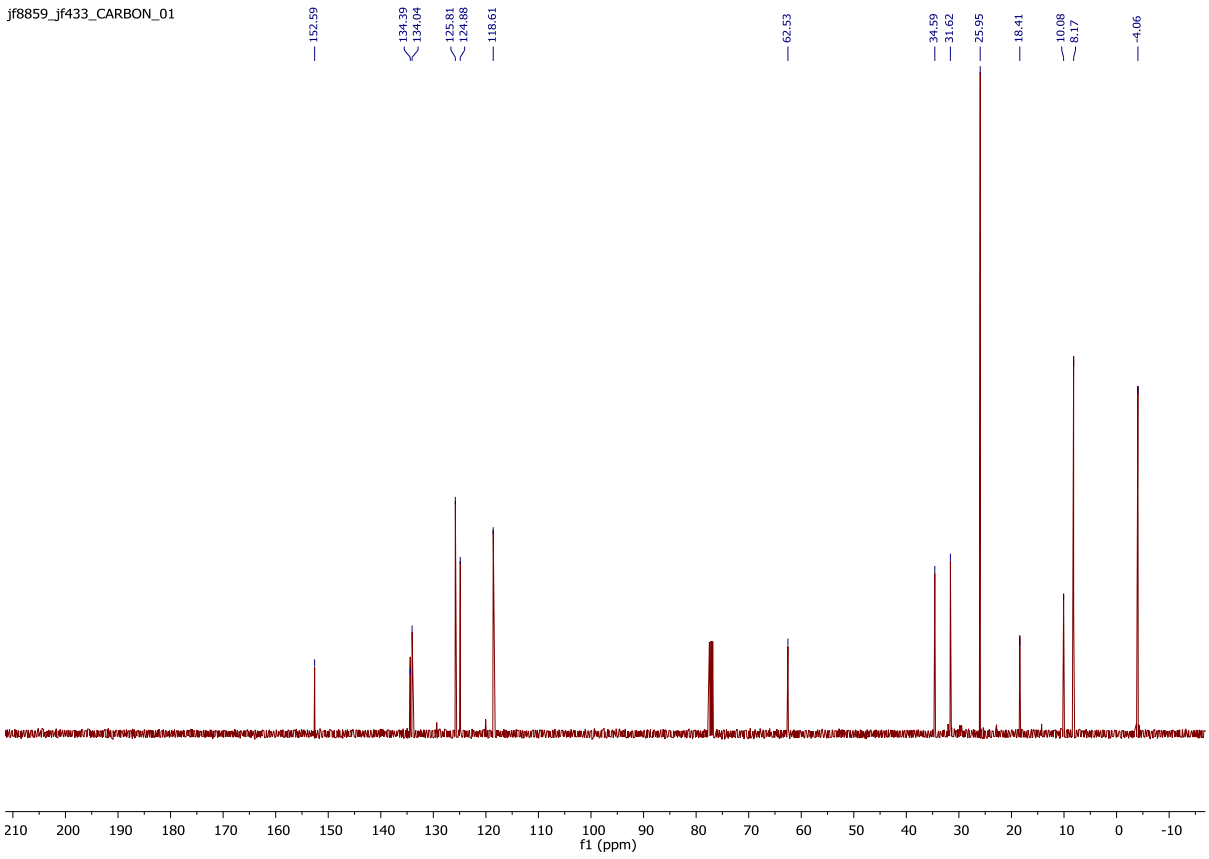
Methyl 3-(4-((*tert*-butyldimethylsilyl)oxy)-3-cyclopropylphenyl)propanoate



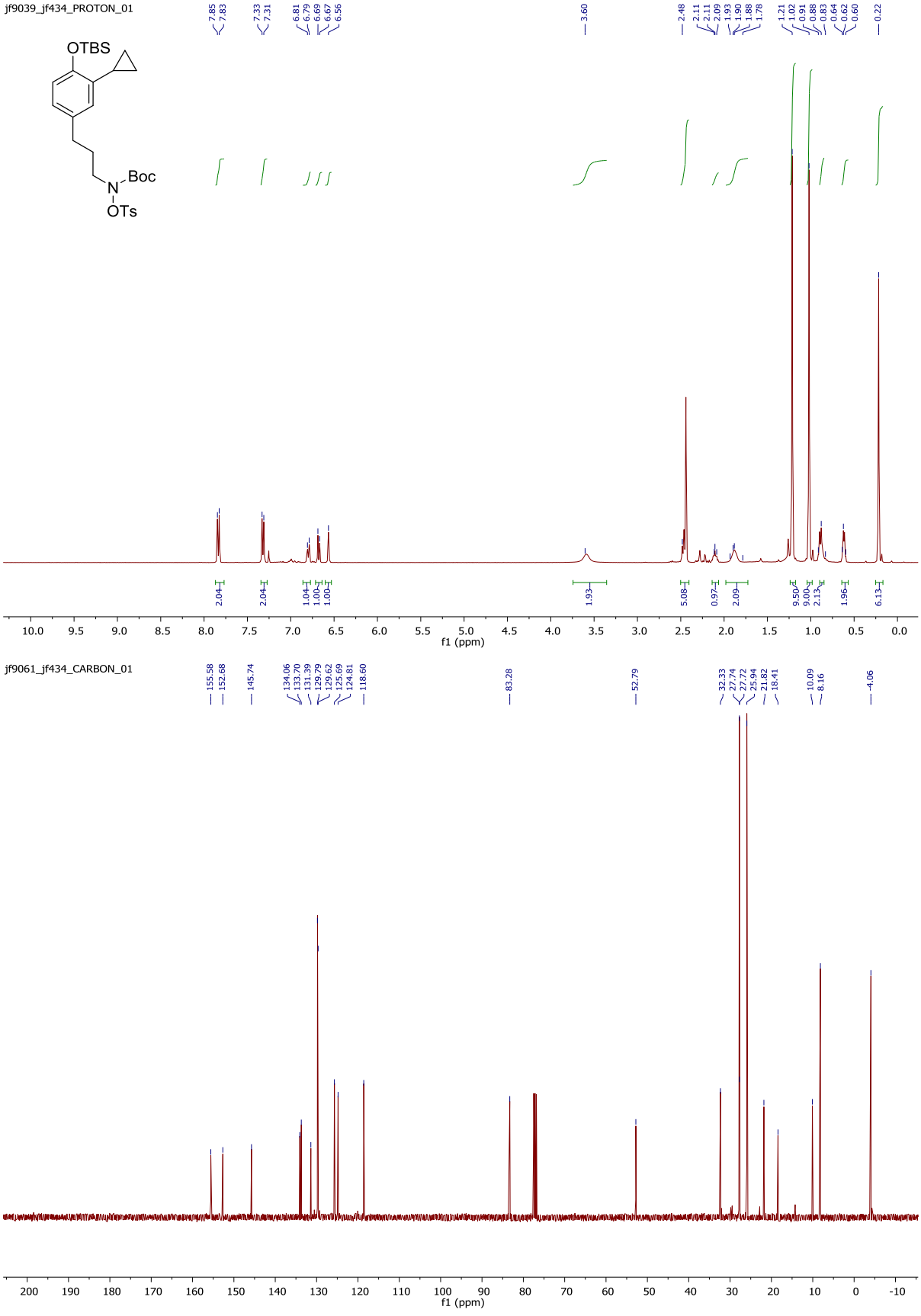


3-(4-((*tert*-Butyldimethylsilyl)oxy)-3-cyclopropylphenyl)propan-1-ol

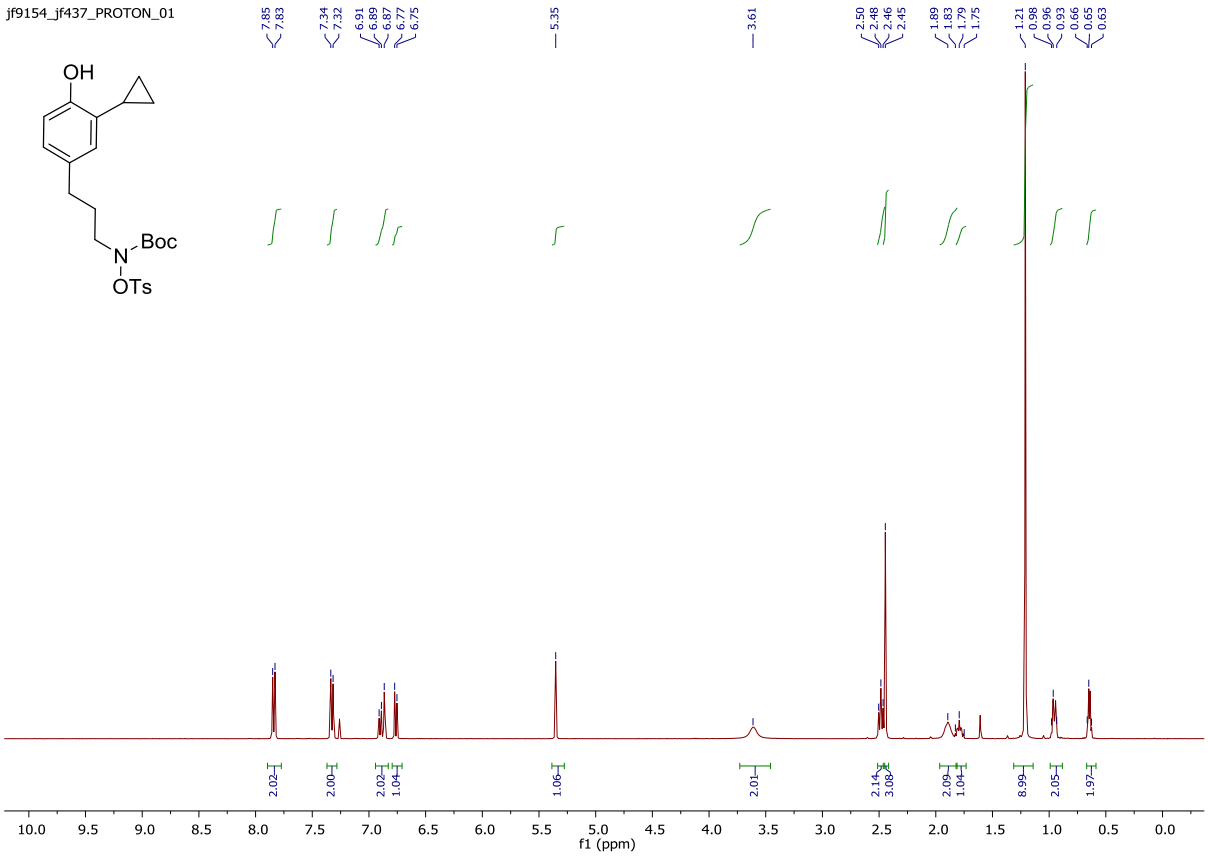


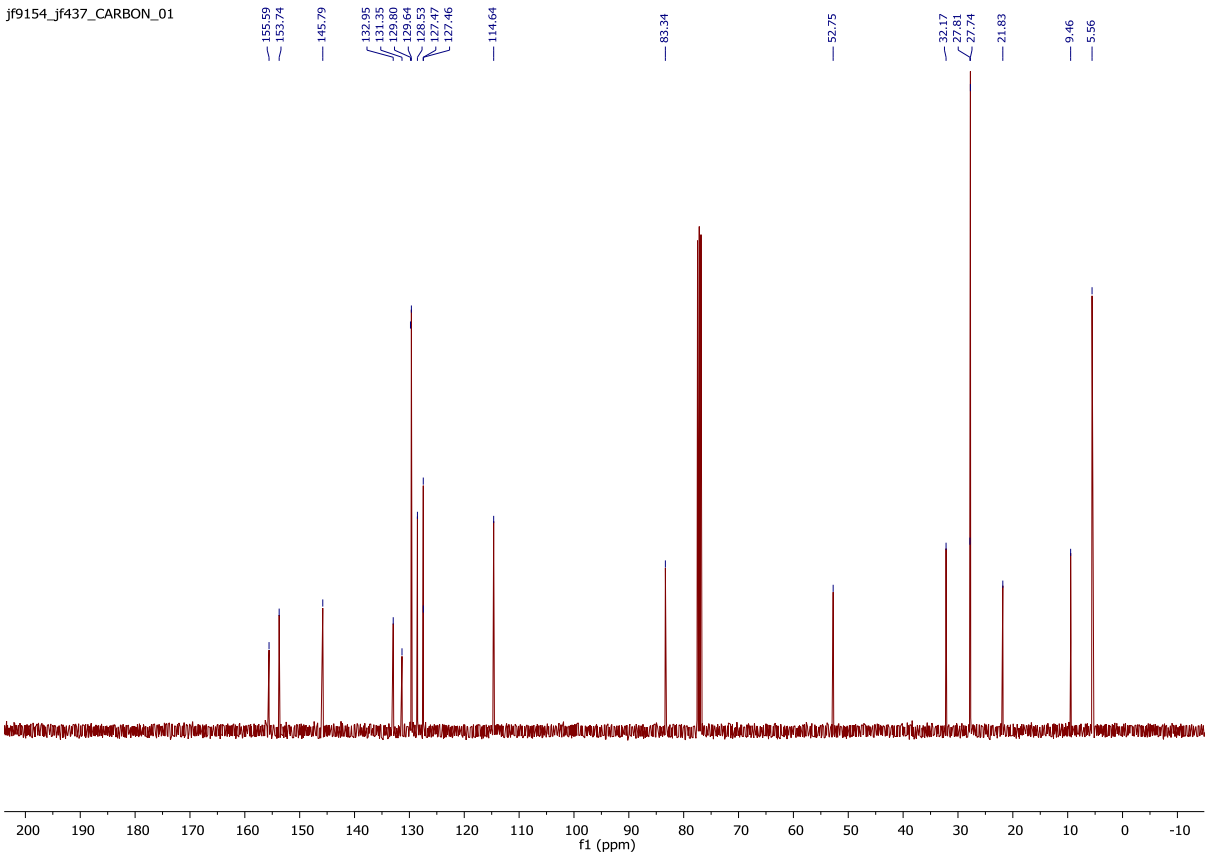


tert-Butyl (3-(4-((_tert_-butyldimethylsilyl)oxy)-3-cyclopropylphenyl)propyl)(tosyloxy) carbamate

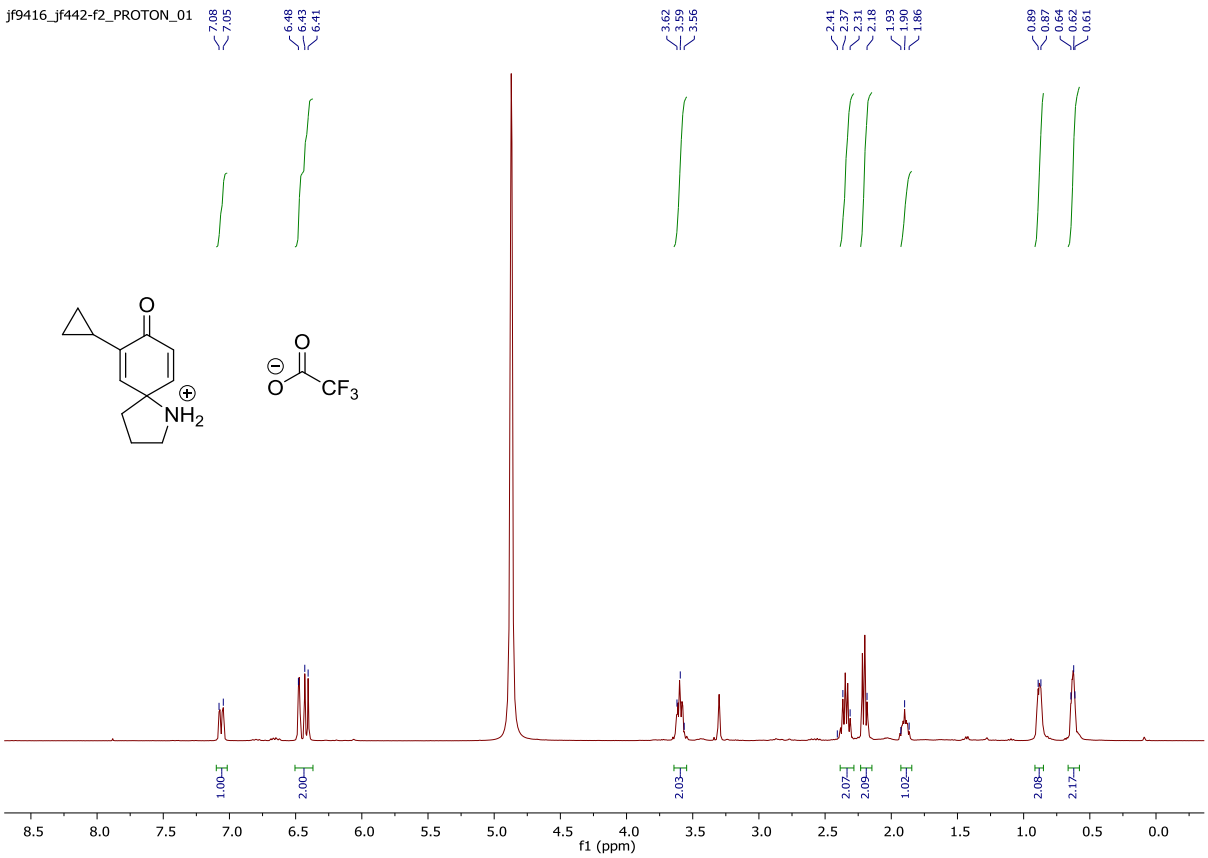


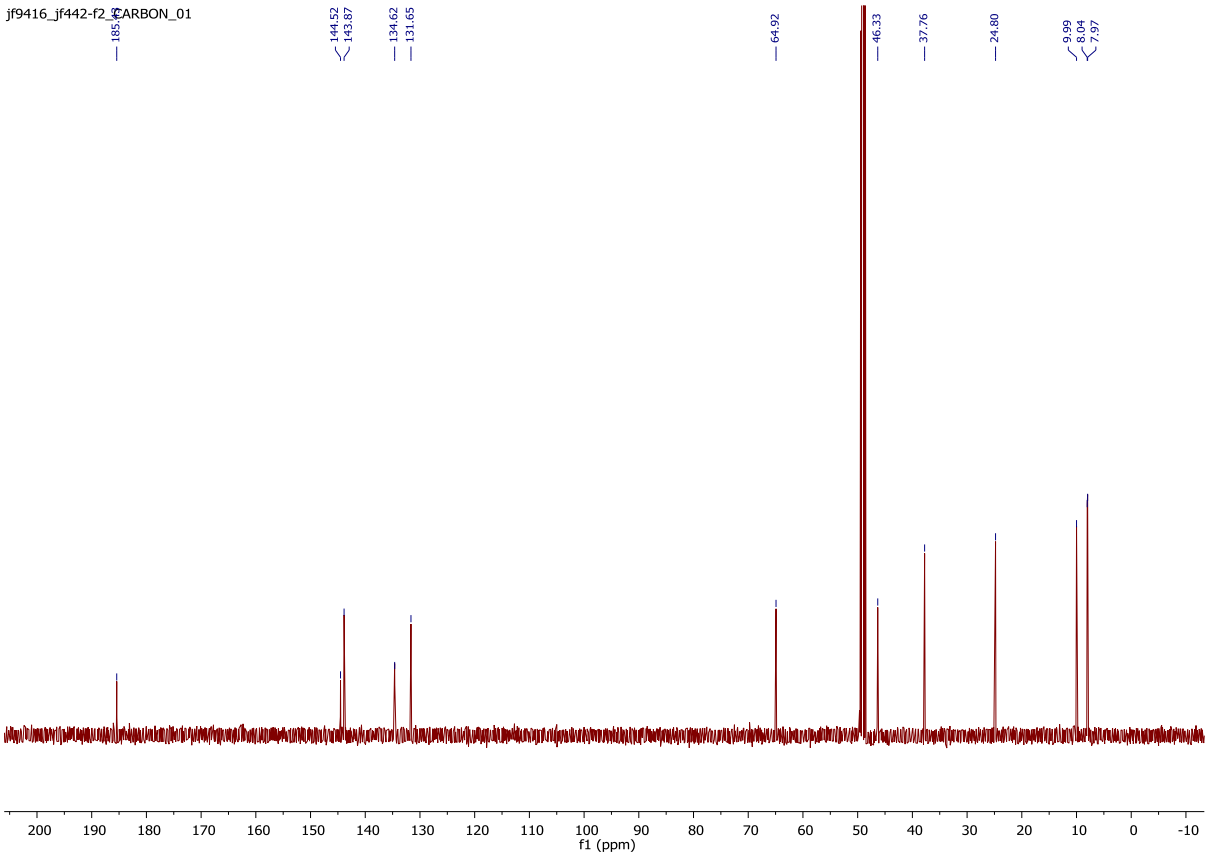
tert-Butyl (3-(3-cyclopropyl-4-hydroxyphenyl)propyl)(tosyloxy)carbamate (5d)



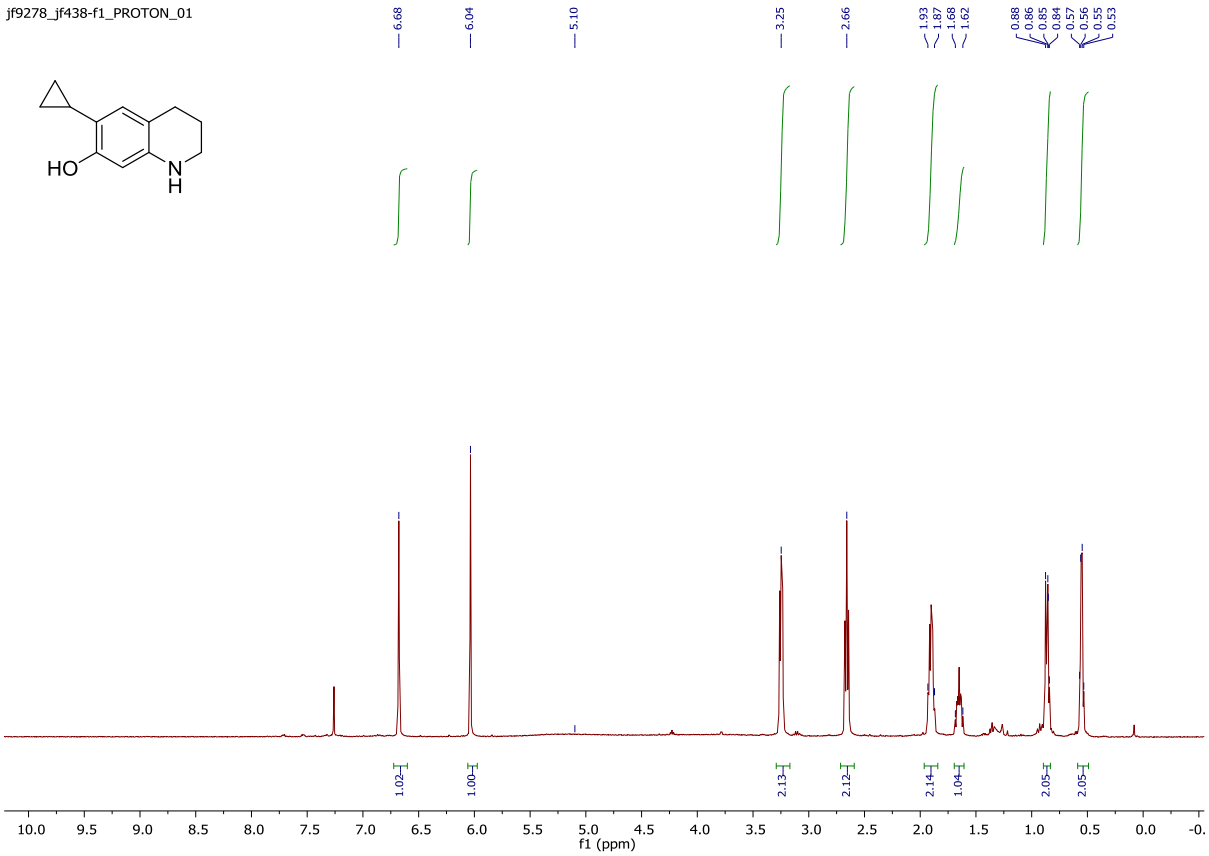


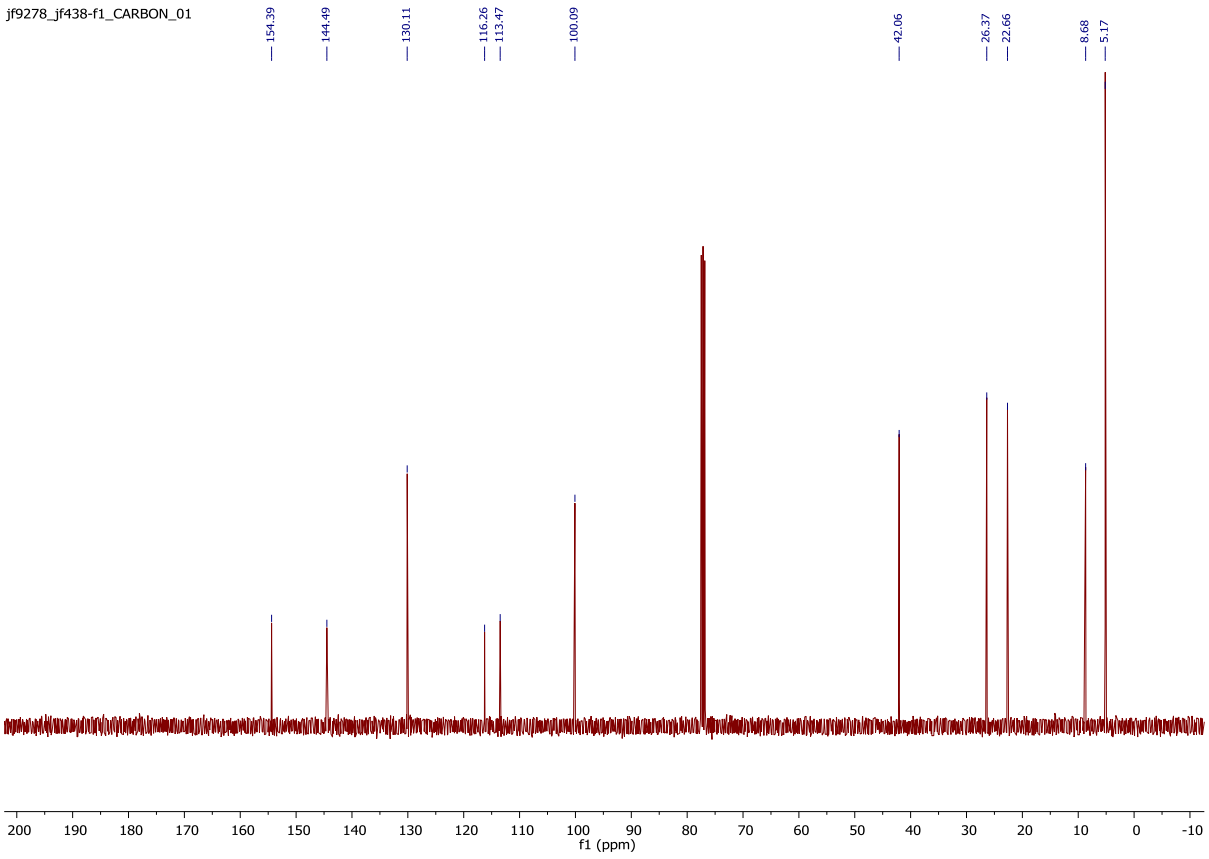
7-Cyclopropyl-1-azaspiro[4.5]deca-6,9-dien-8-one trifluoroacetate (7d)



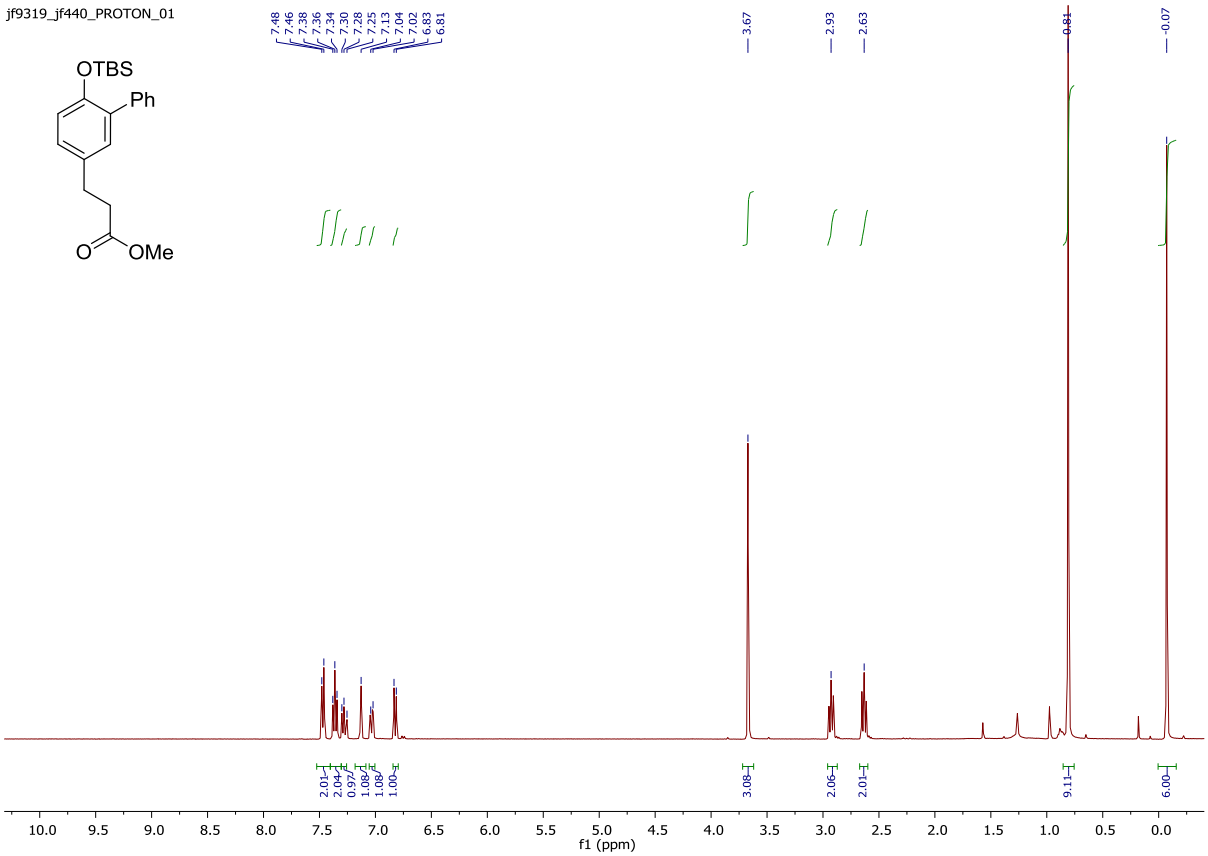


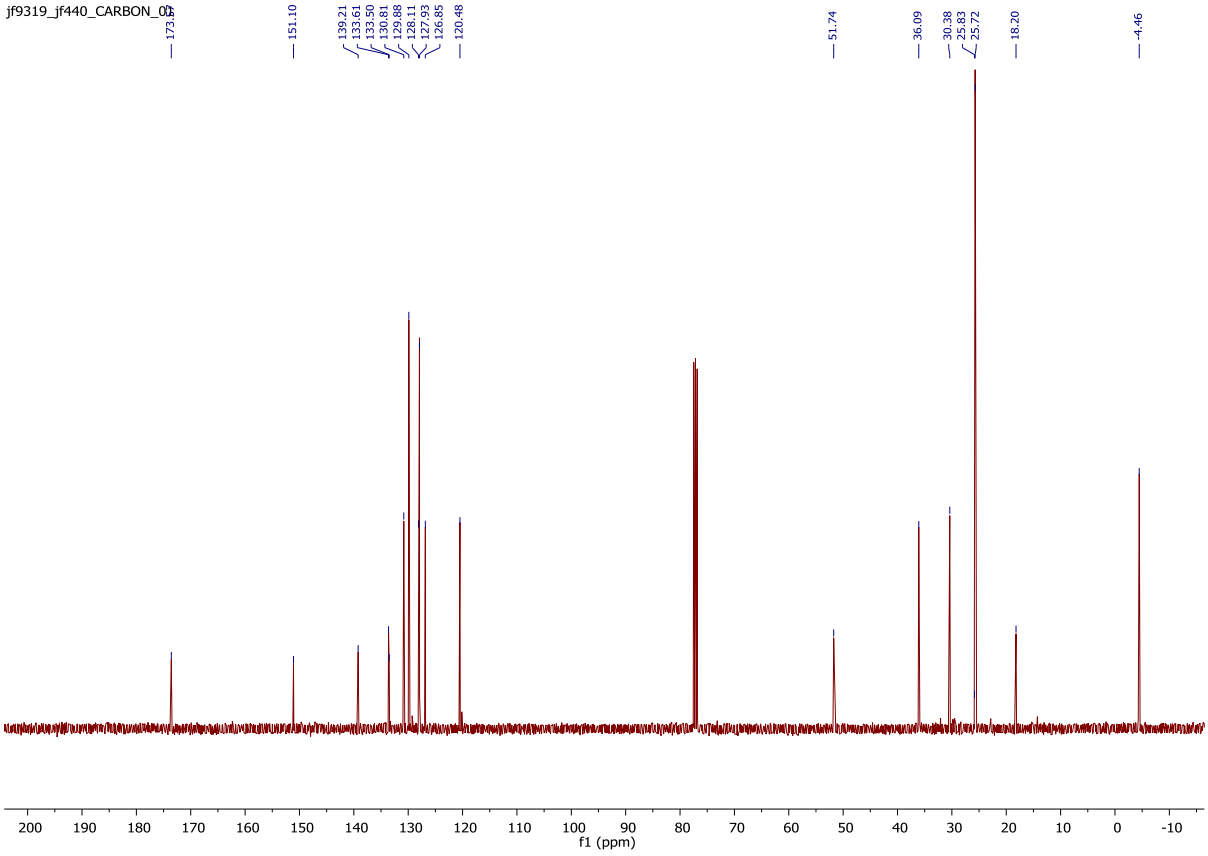
6-cyclopropyl-1,2,3,4-tetrahydroquinolin-7-ol (8d)



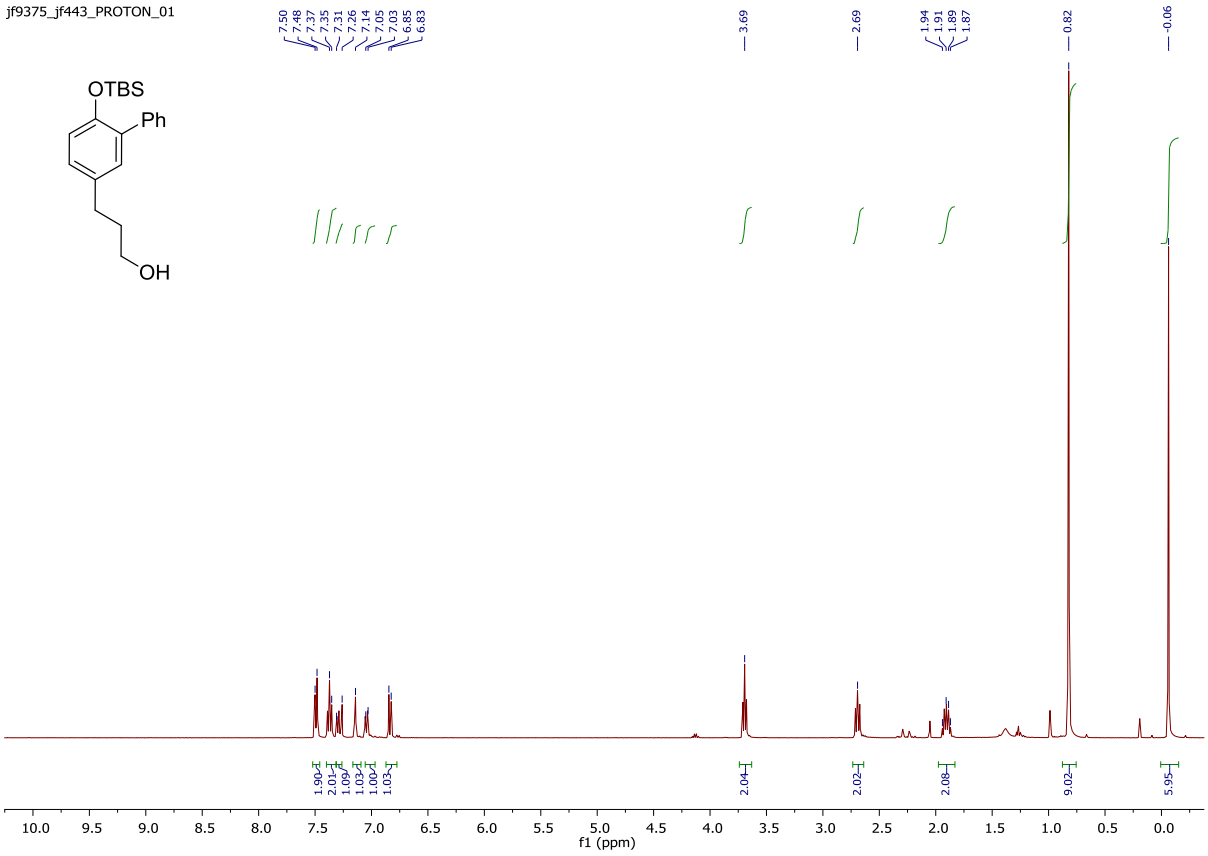


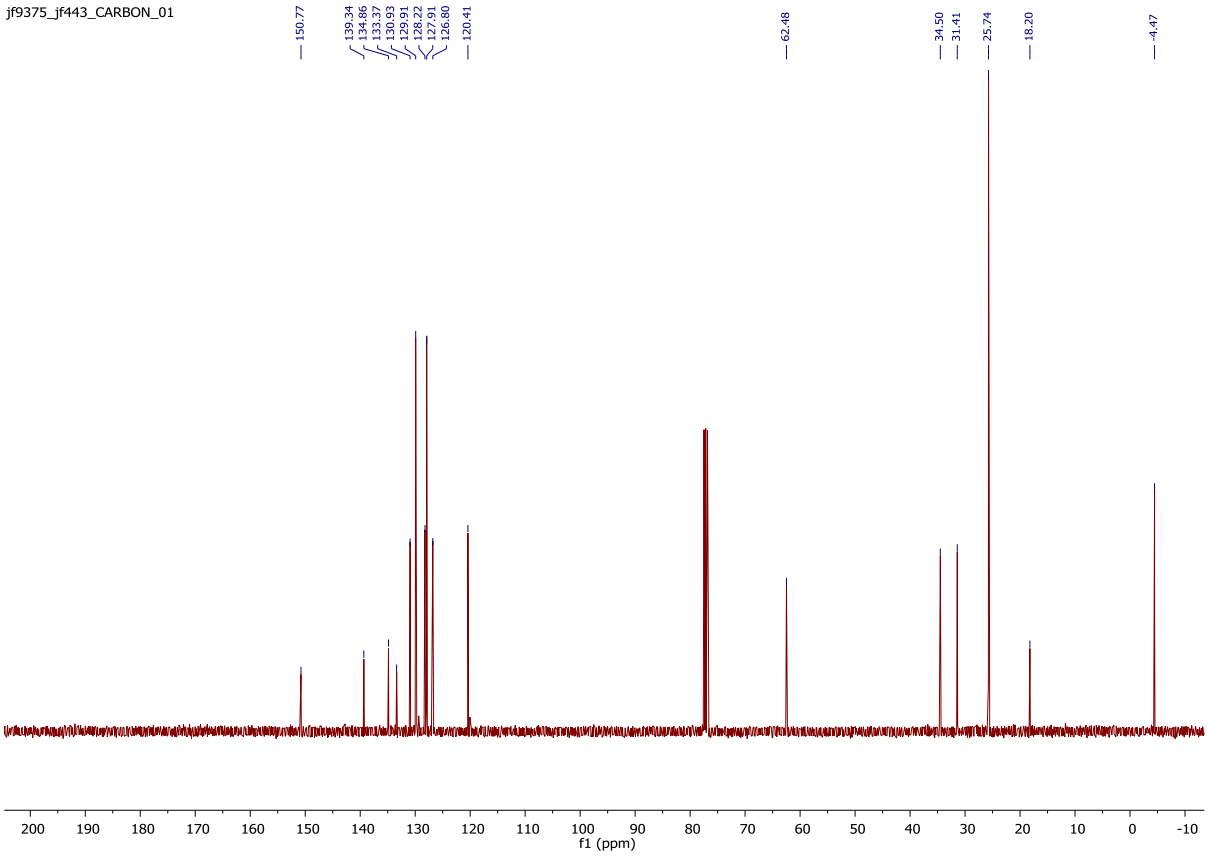
Methyl3-(6-((*tert*-butyldimethylsilyl)oxy)-[1,1'-biphenyl]-3-yl)propanoate



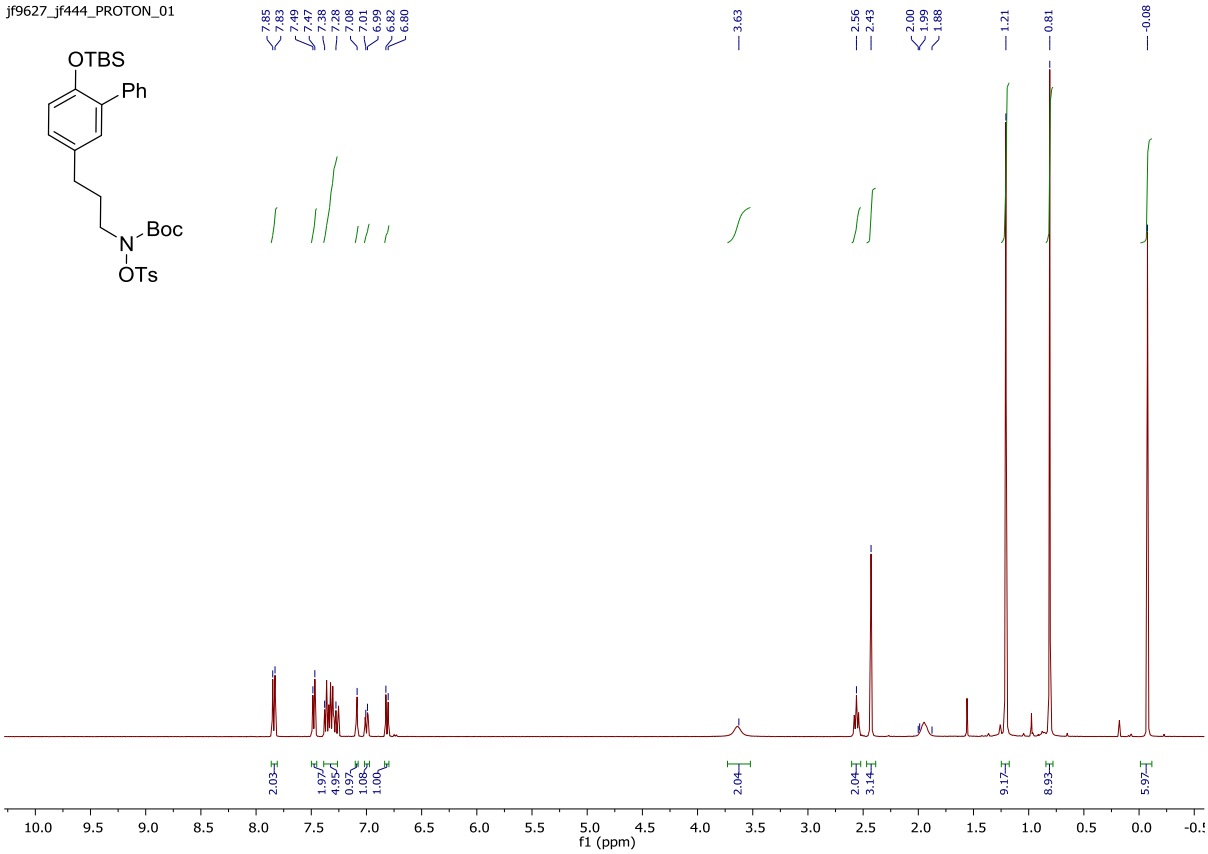


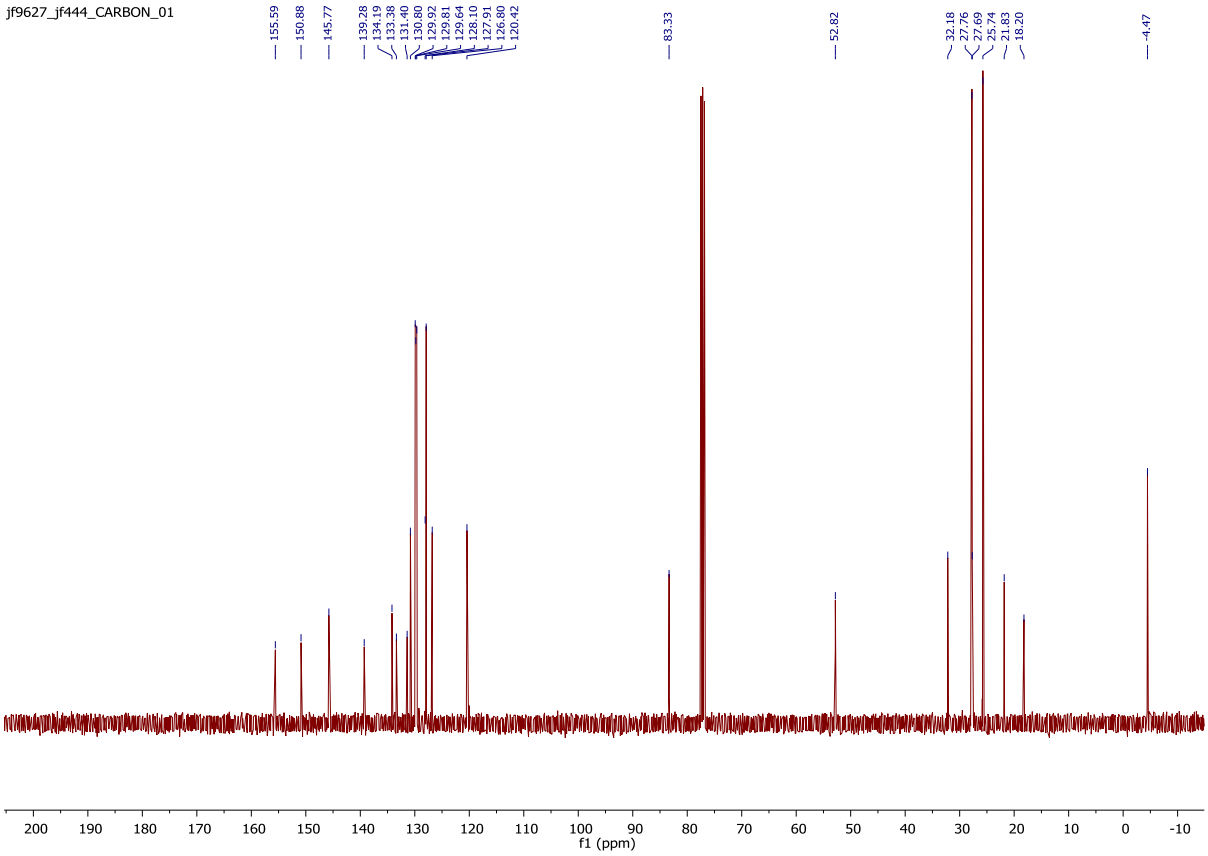
3-(6-((*tert*-Butyldimethylsilyl)oxy)-[1,1'-biphenyl]-3-yl)propan-1-ol



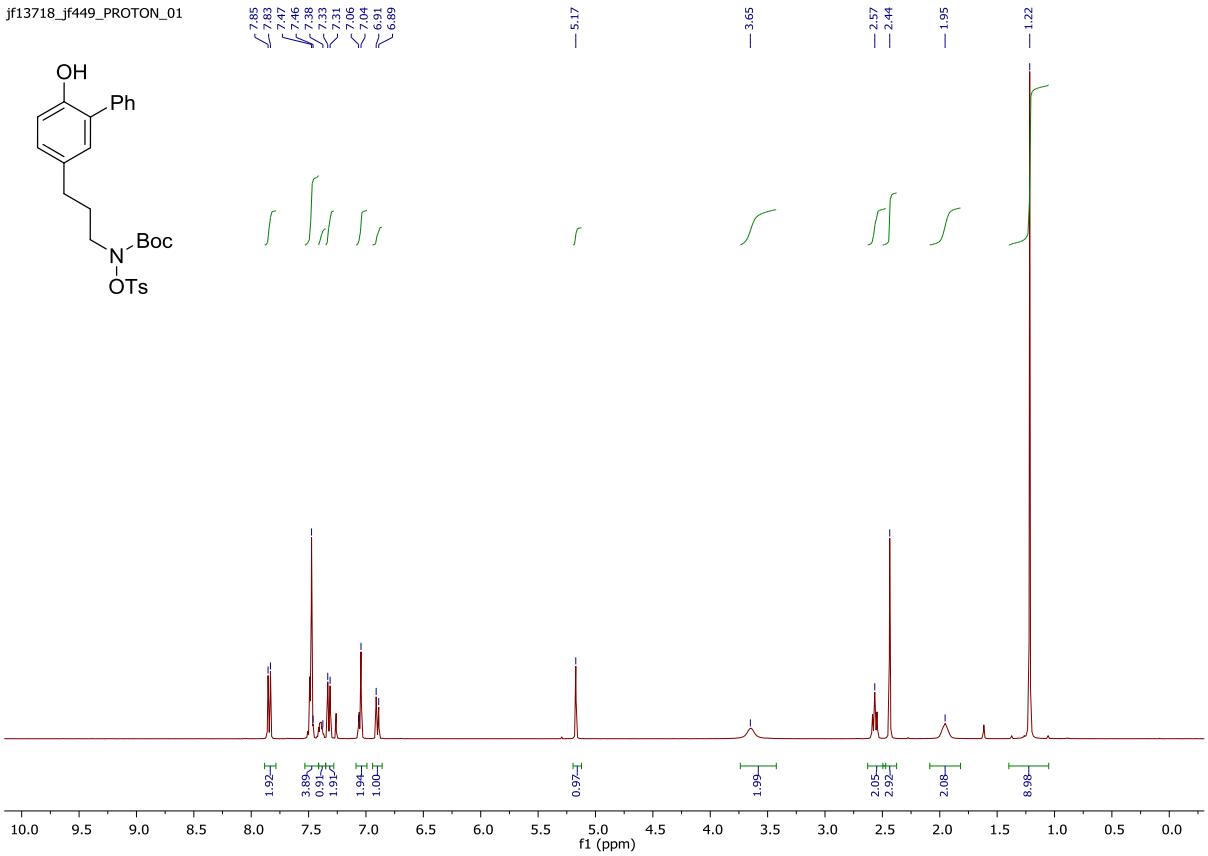


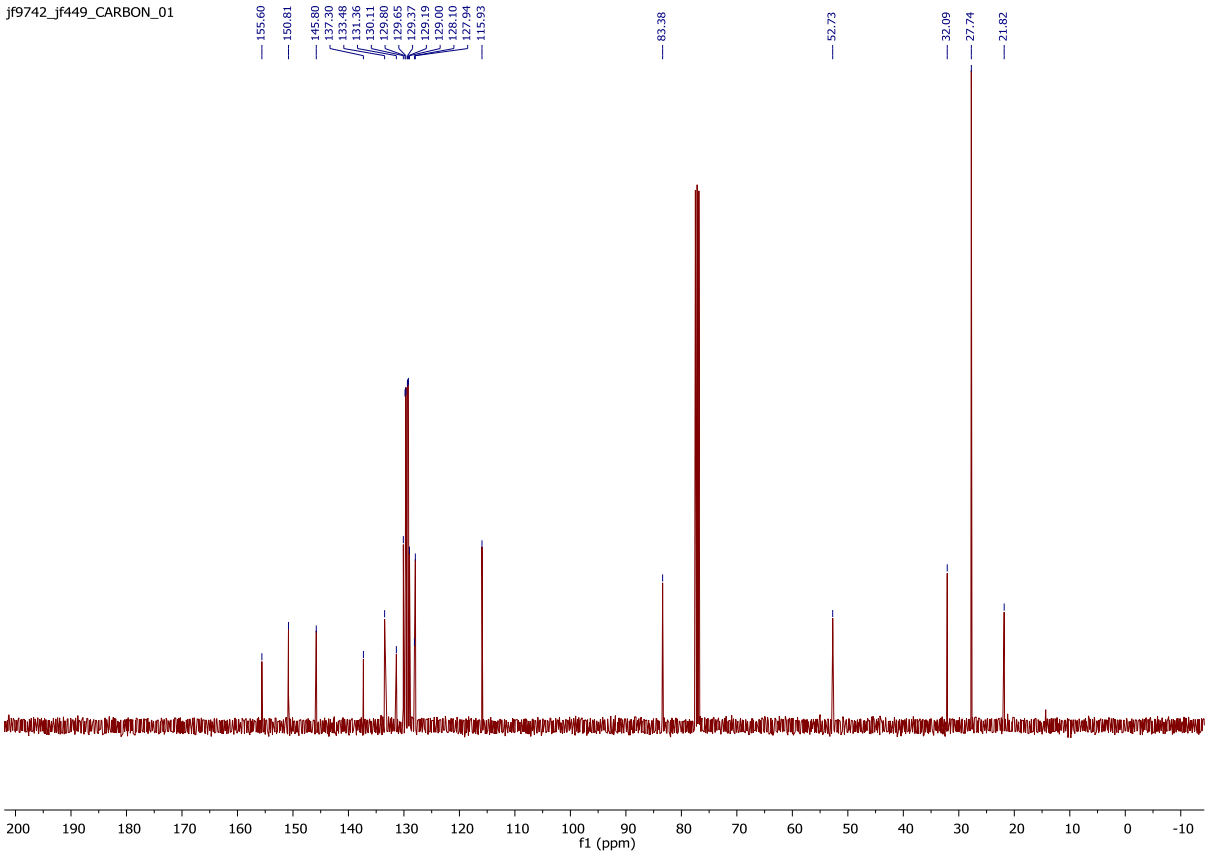
tert-Butyl(3-(6-((_tert_-butyldimethylsilyl)oxy)-[1,1'-biphenyl]-3-yl)propyl)(tosyloxy) carbamate



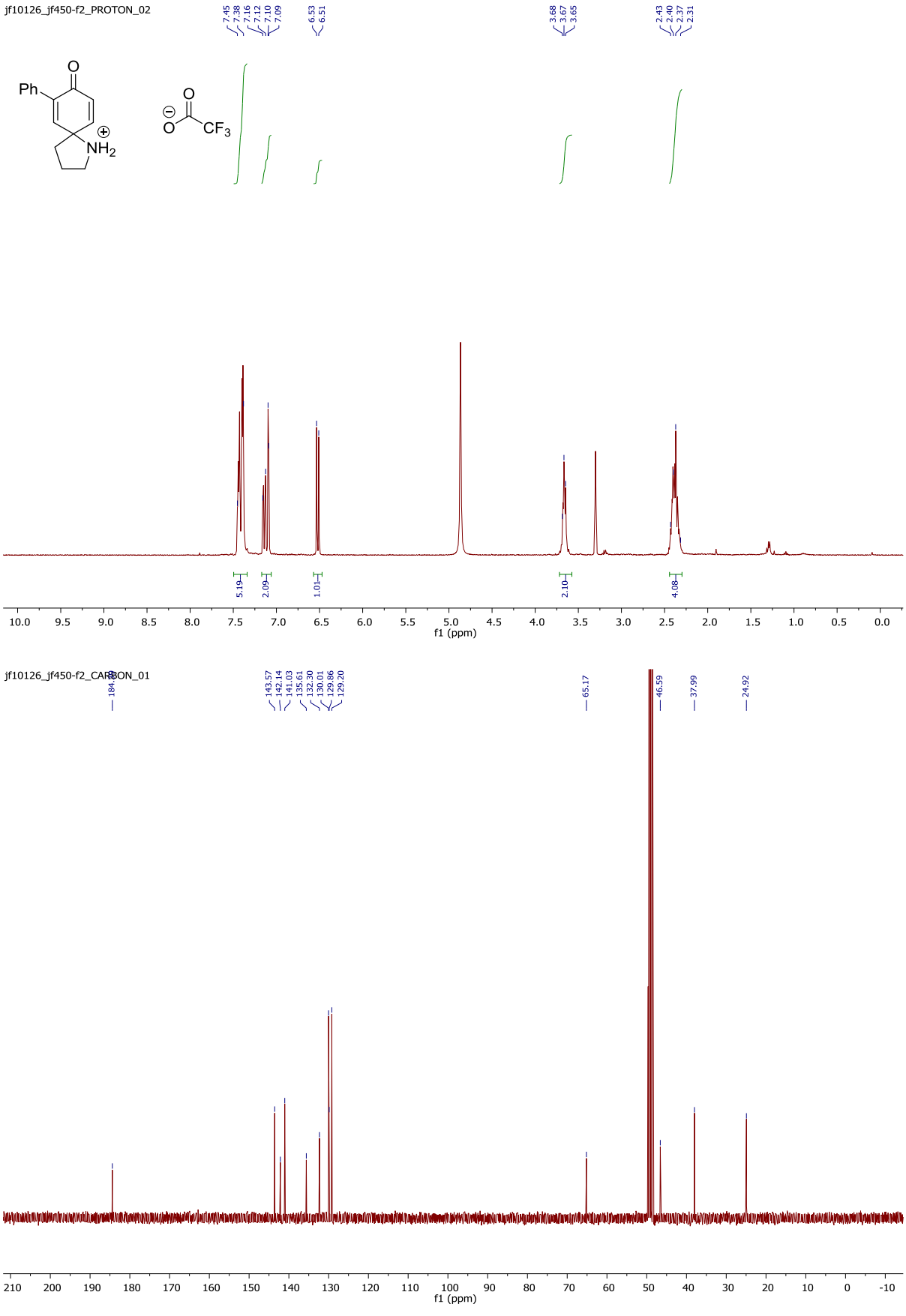


tert-Butyl (3-(6-hydroxy-[1,1'-biphenyl]-3-yl)propyl)(tosyloxy)carbamate (5e)

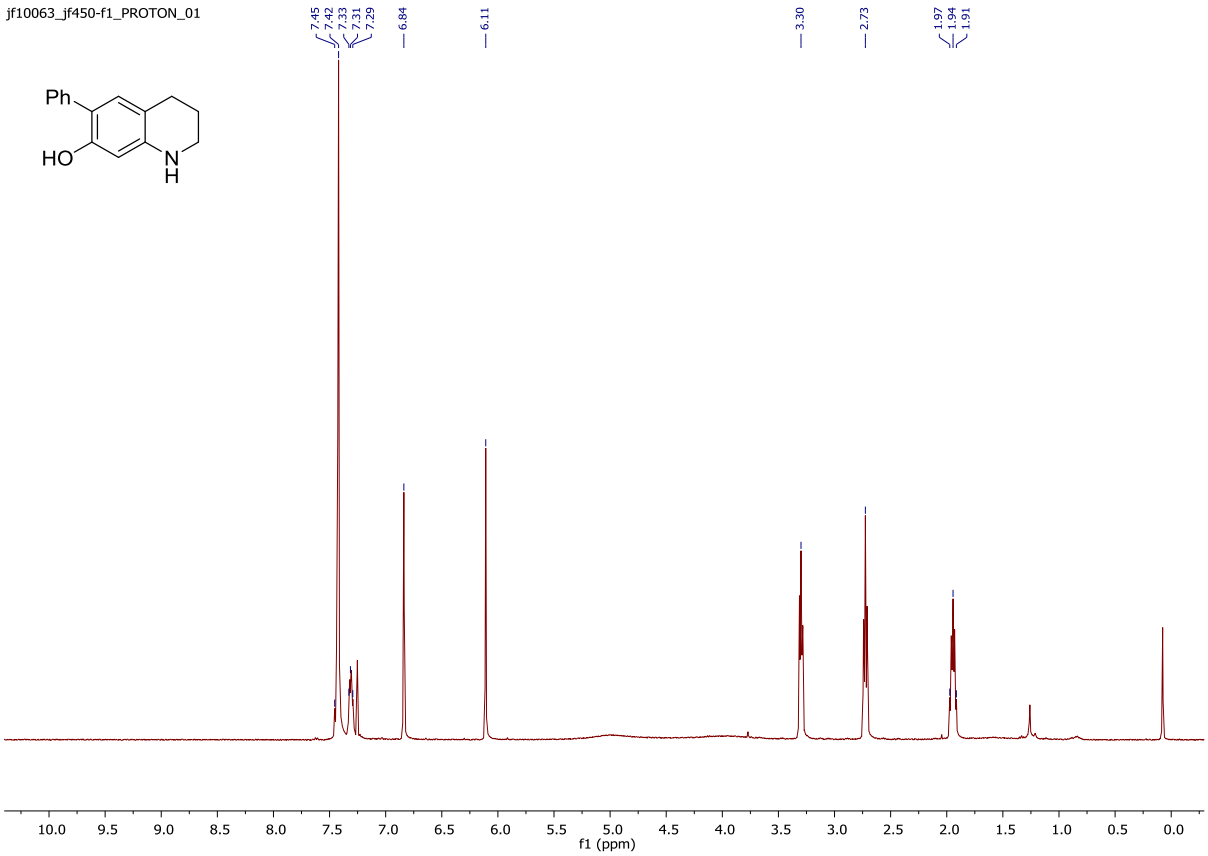


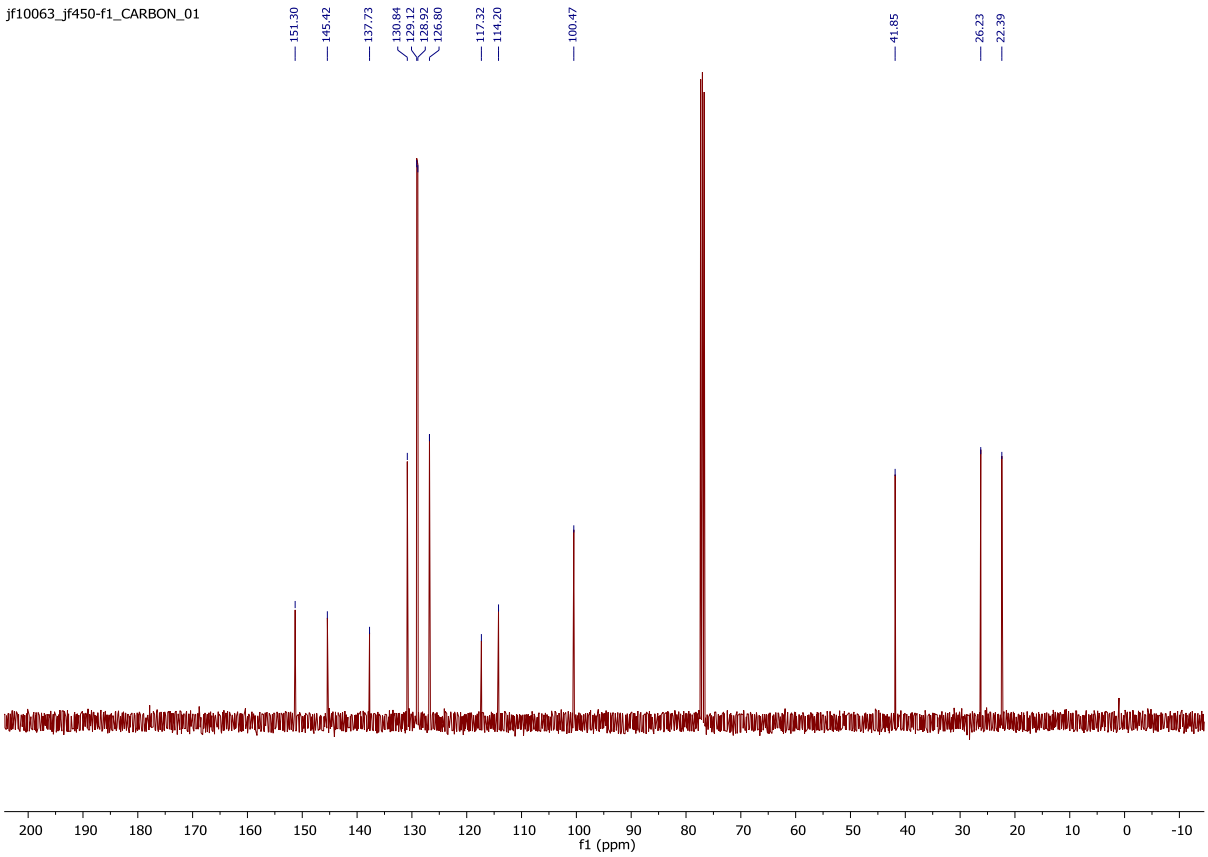


7-Phenyl-1-azaspiro[4.5]deca-6,9-dien-8-one trifluoroacetate (7e)

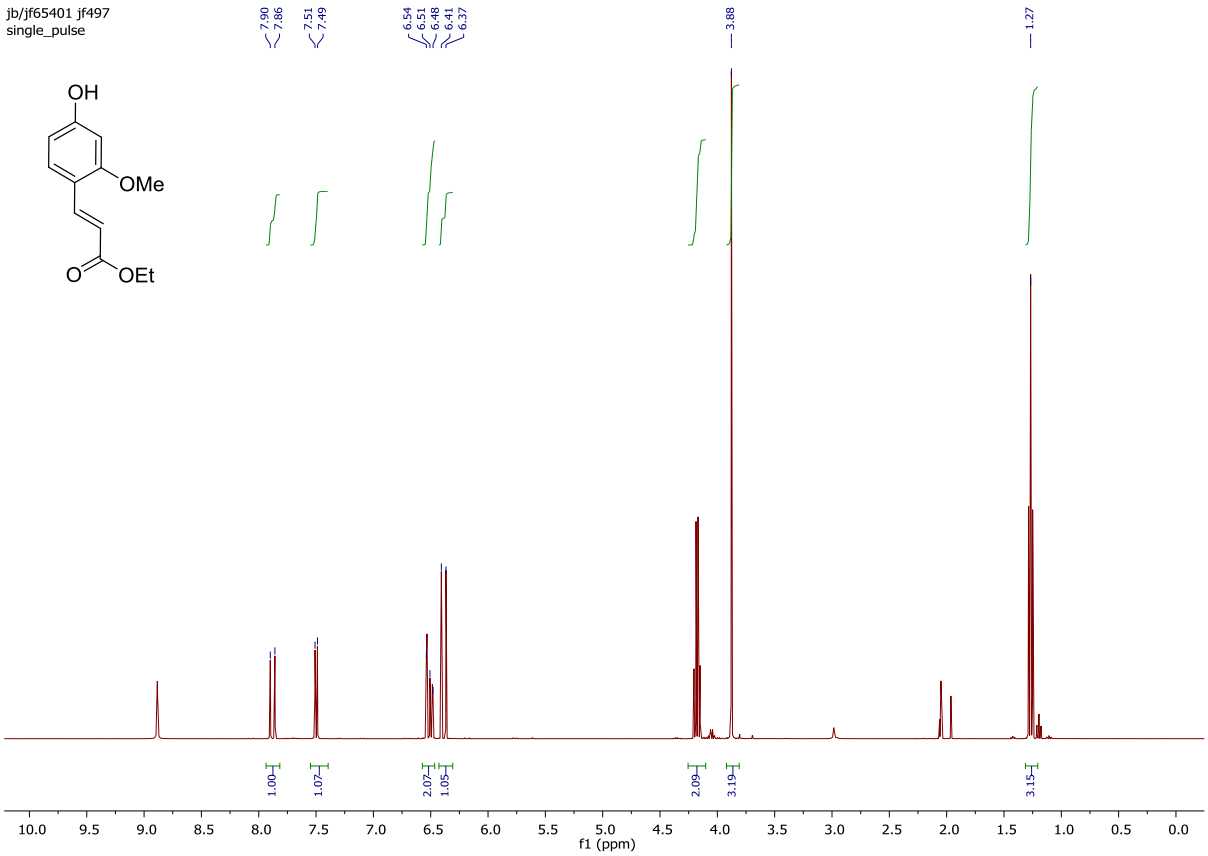


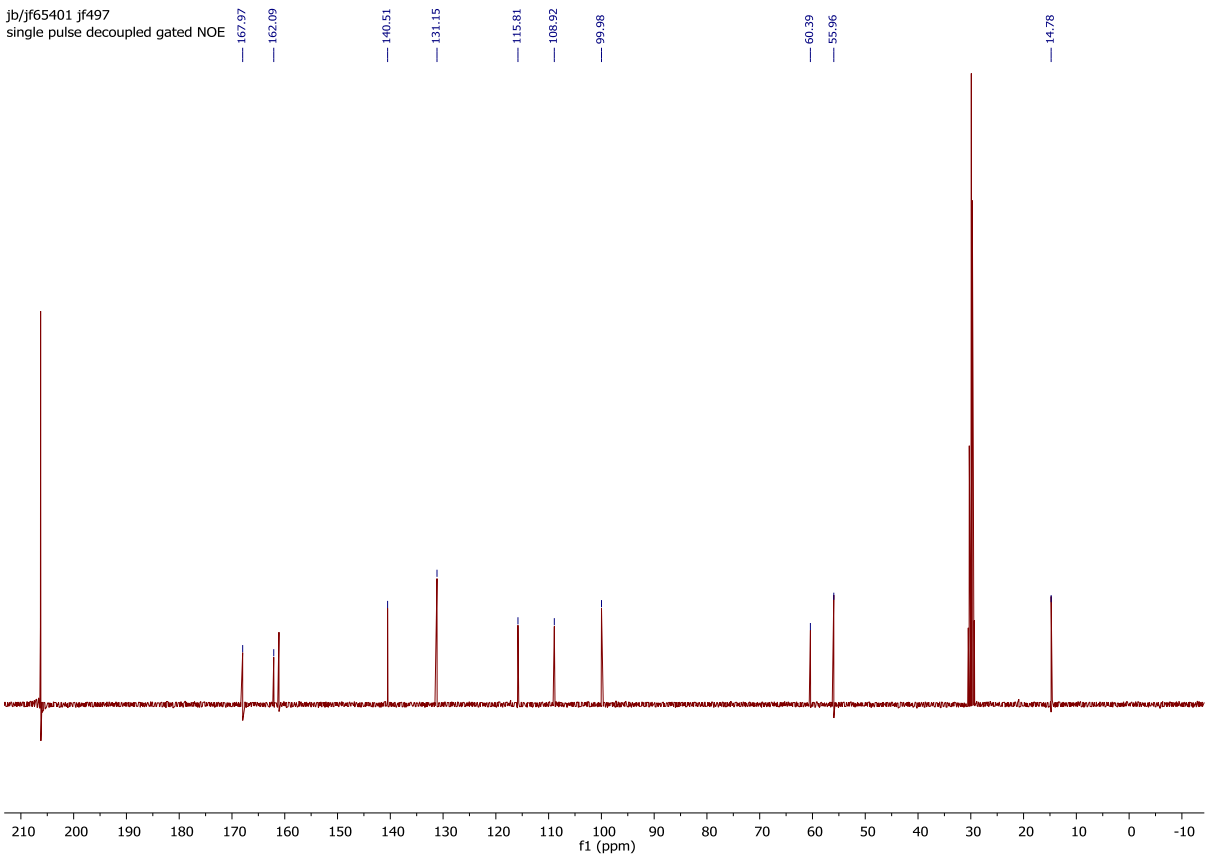
6-Phenyl-1,2,3,4-tetrahydroquinolin-7-ol (8e)



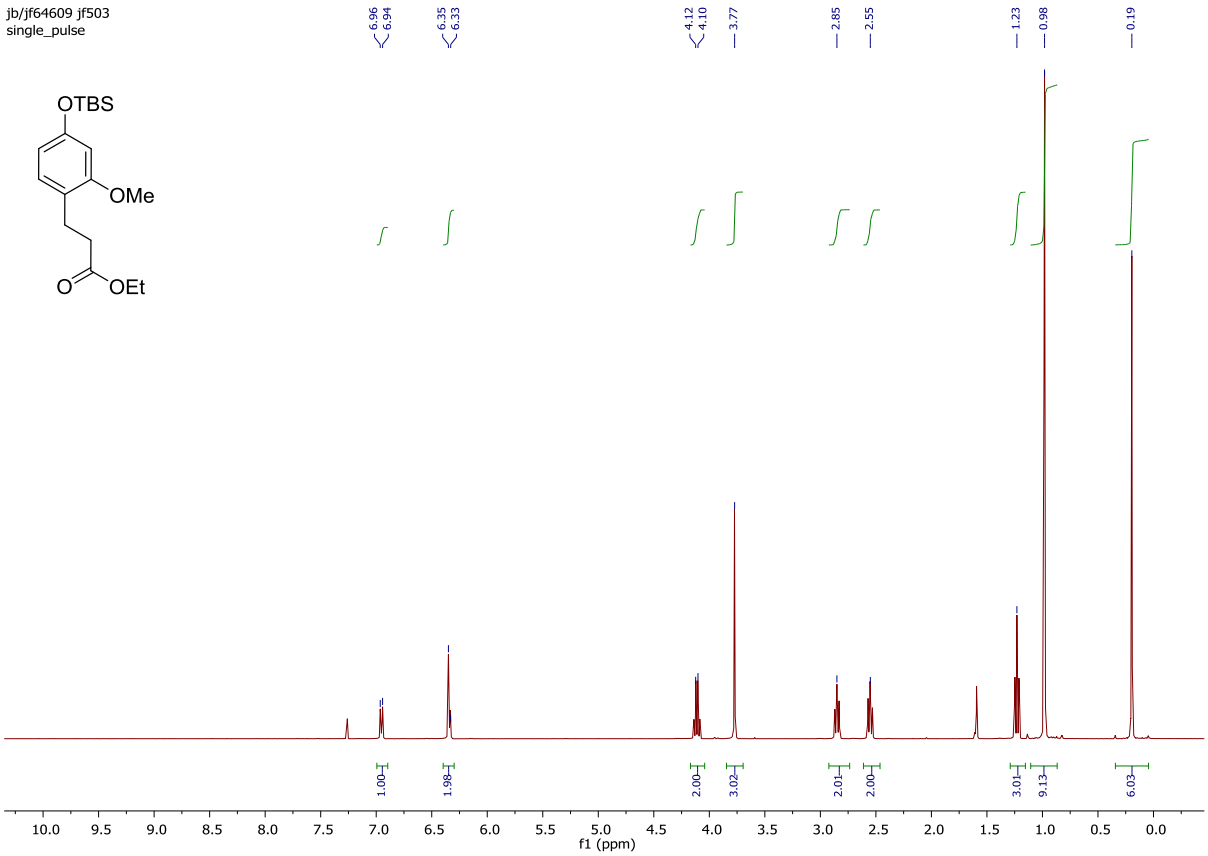


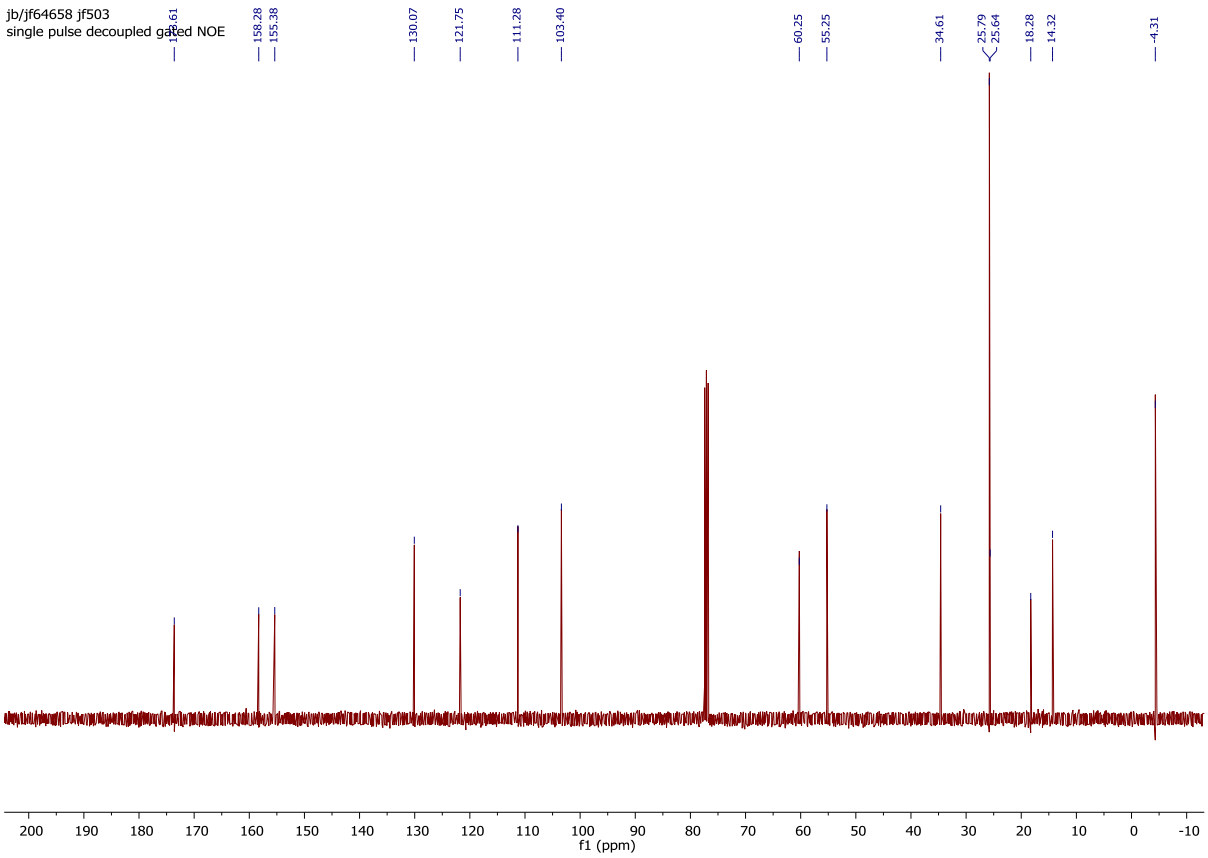
Ethyl (*E*)-3-(4-hydroxy-2-methoxyphenyl)acrylate



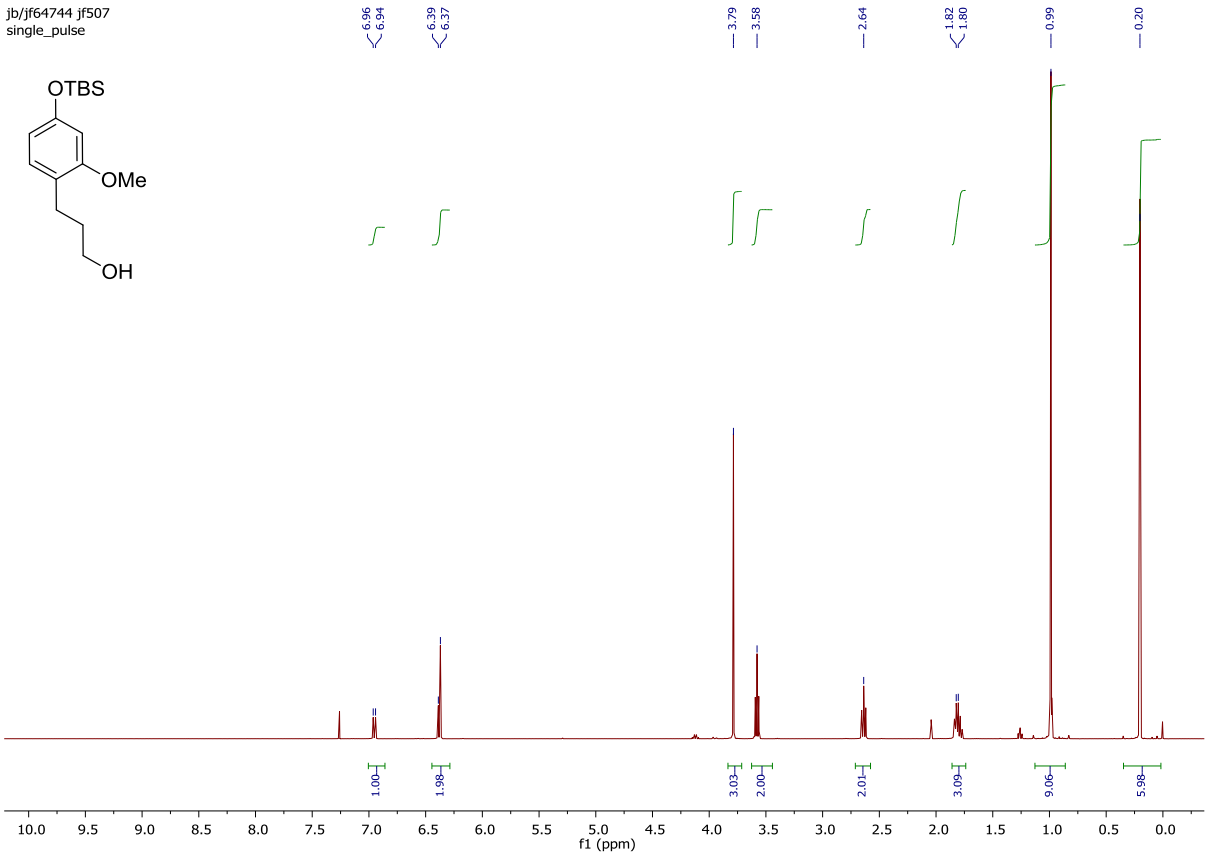


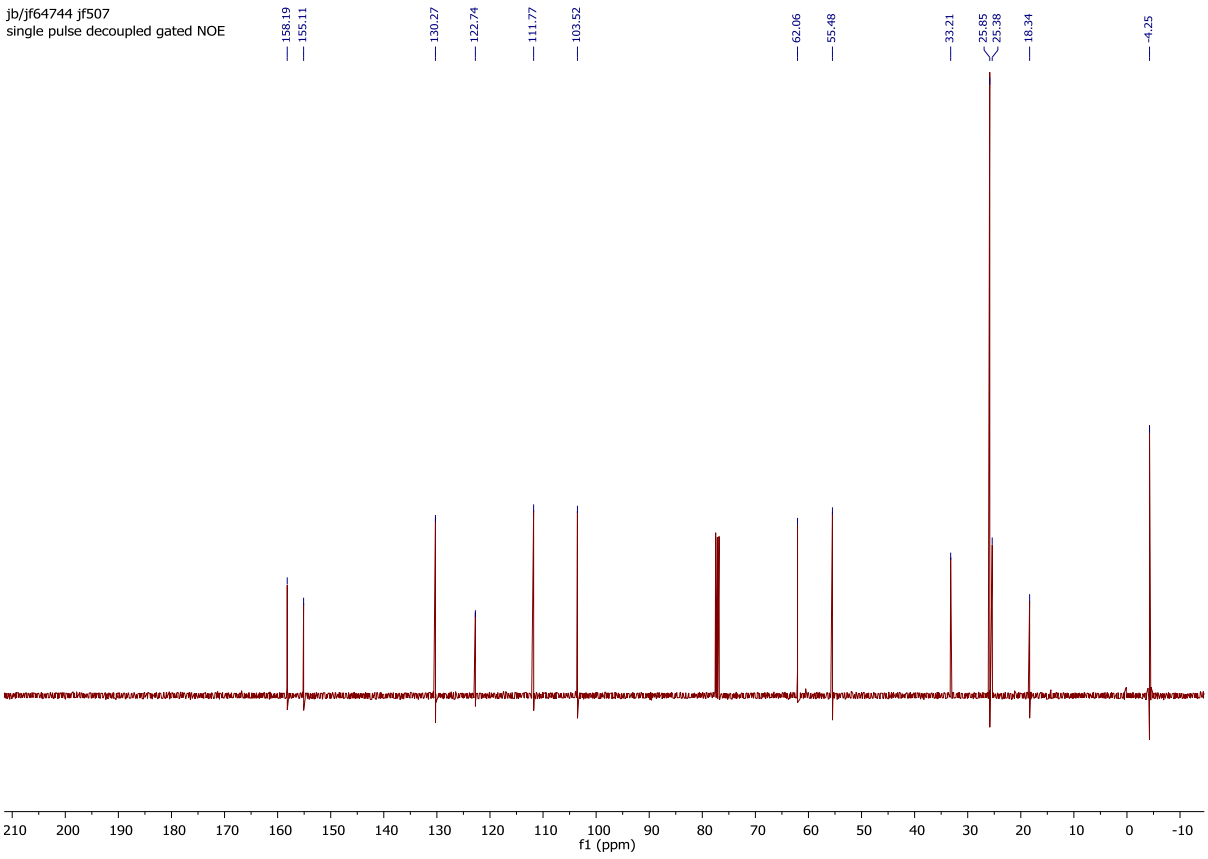
Ethyl 3-(4-((*tert*-butyldimethylsilyl)oxy)-2-methoxyphenyl)propanoate



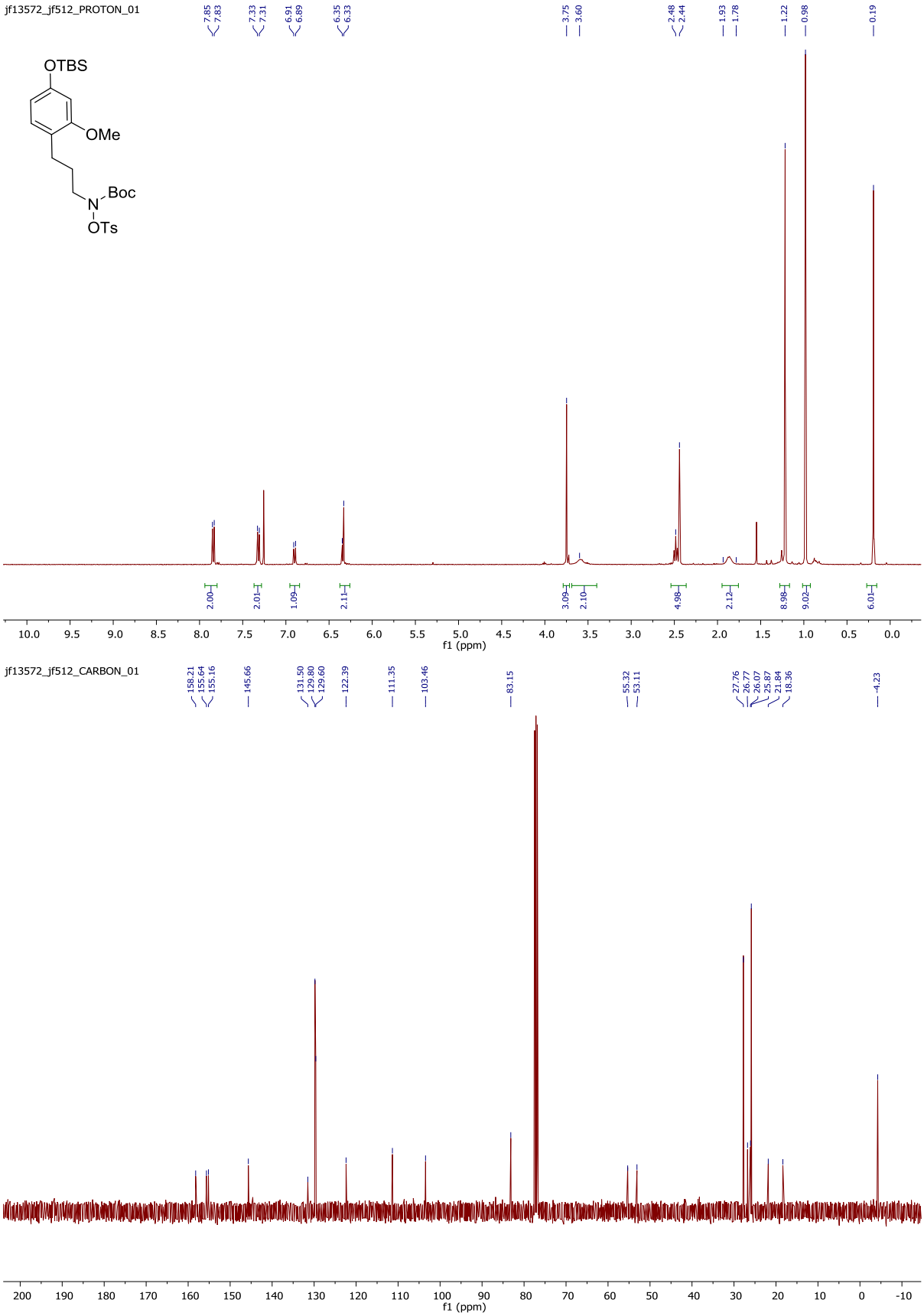


3-(4-((*tert*-Butyldimethylsilyl)oxy)-2-methoxyphenyl)propan-1-ol

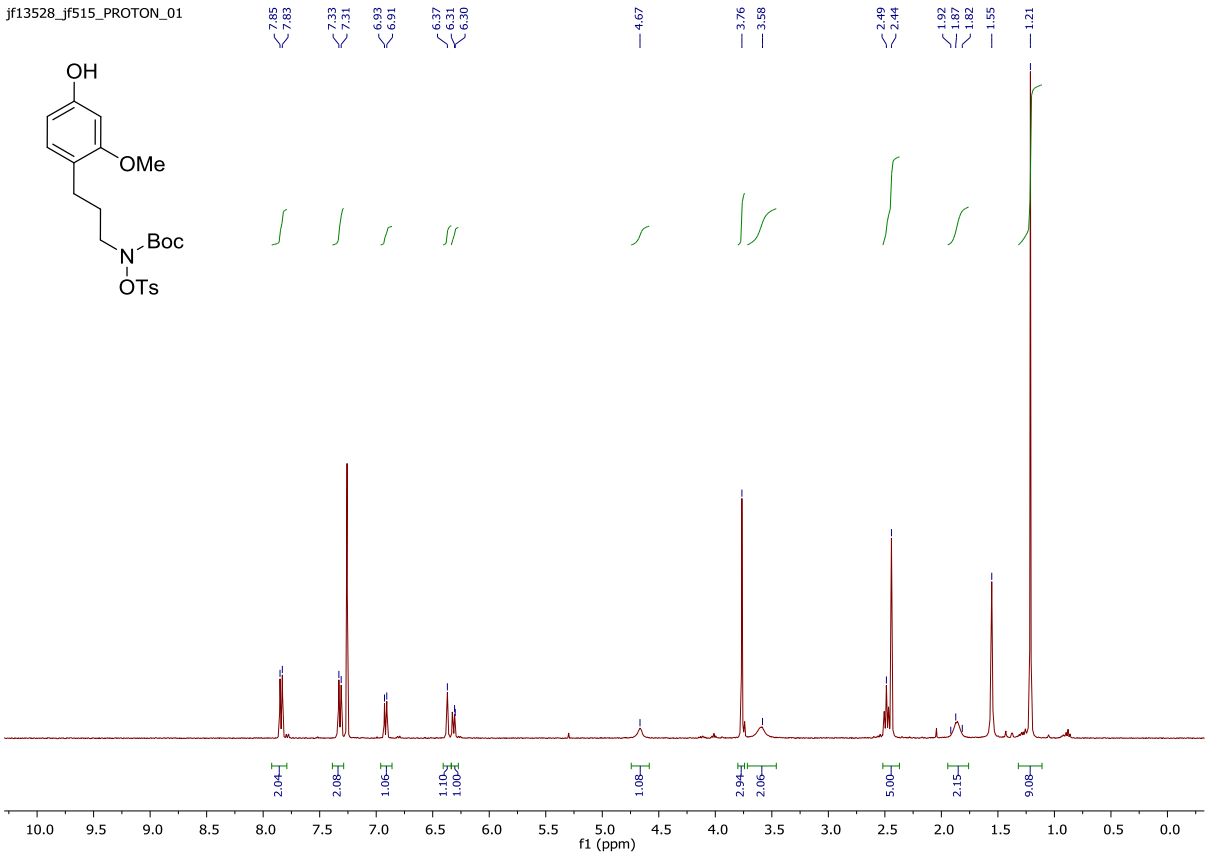


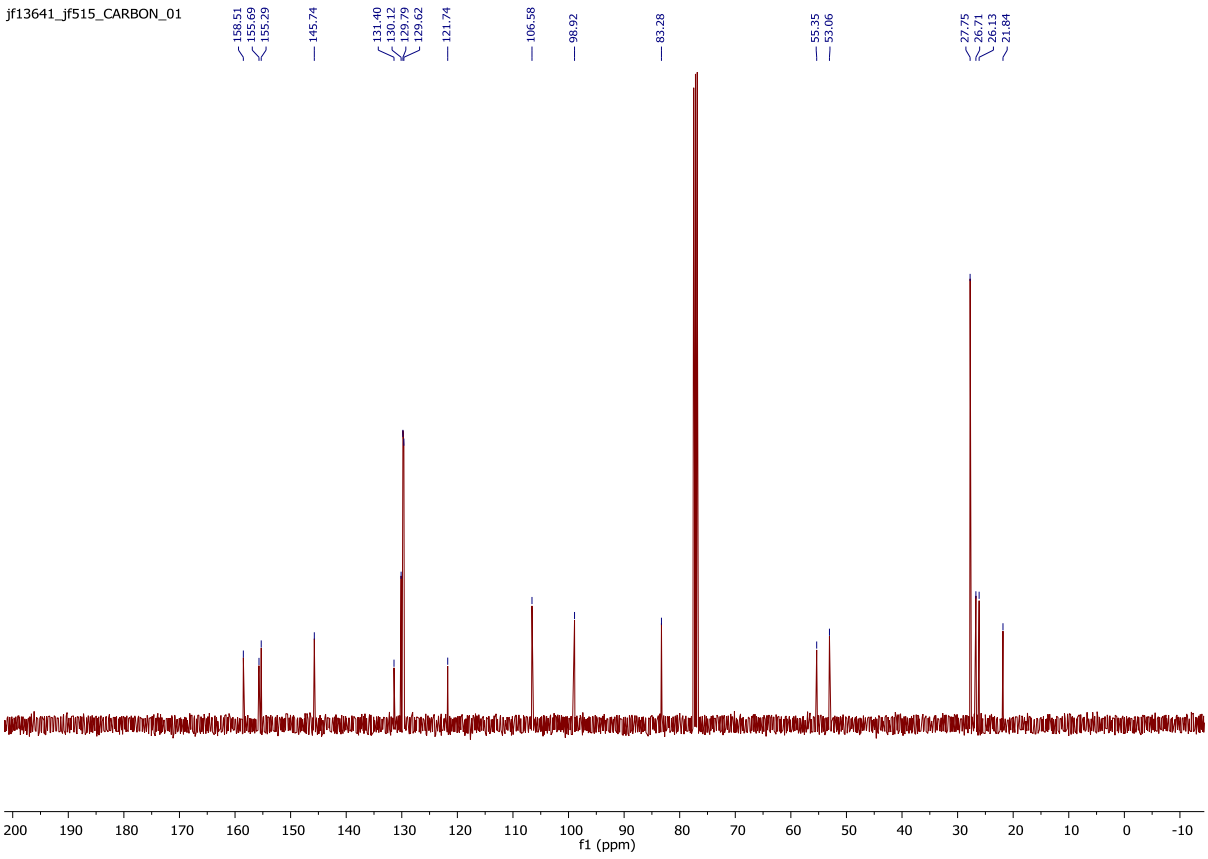


tert-Butyl (3-(4-((_tert_-butyldimethylsilyl)oxy)-2-methoxyphenyl)propyl)(tosyloxy) carbamate

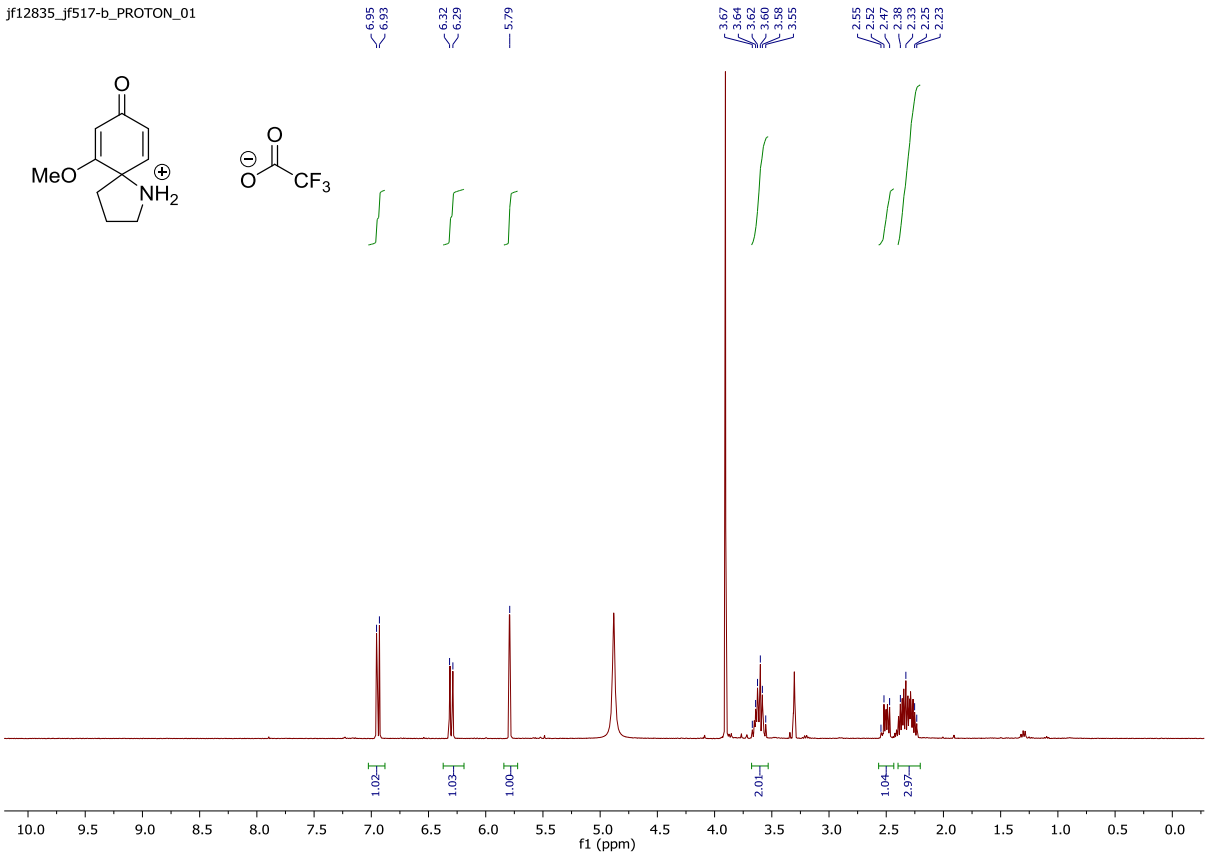


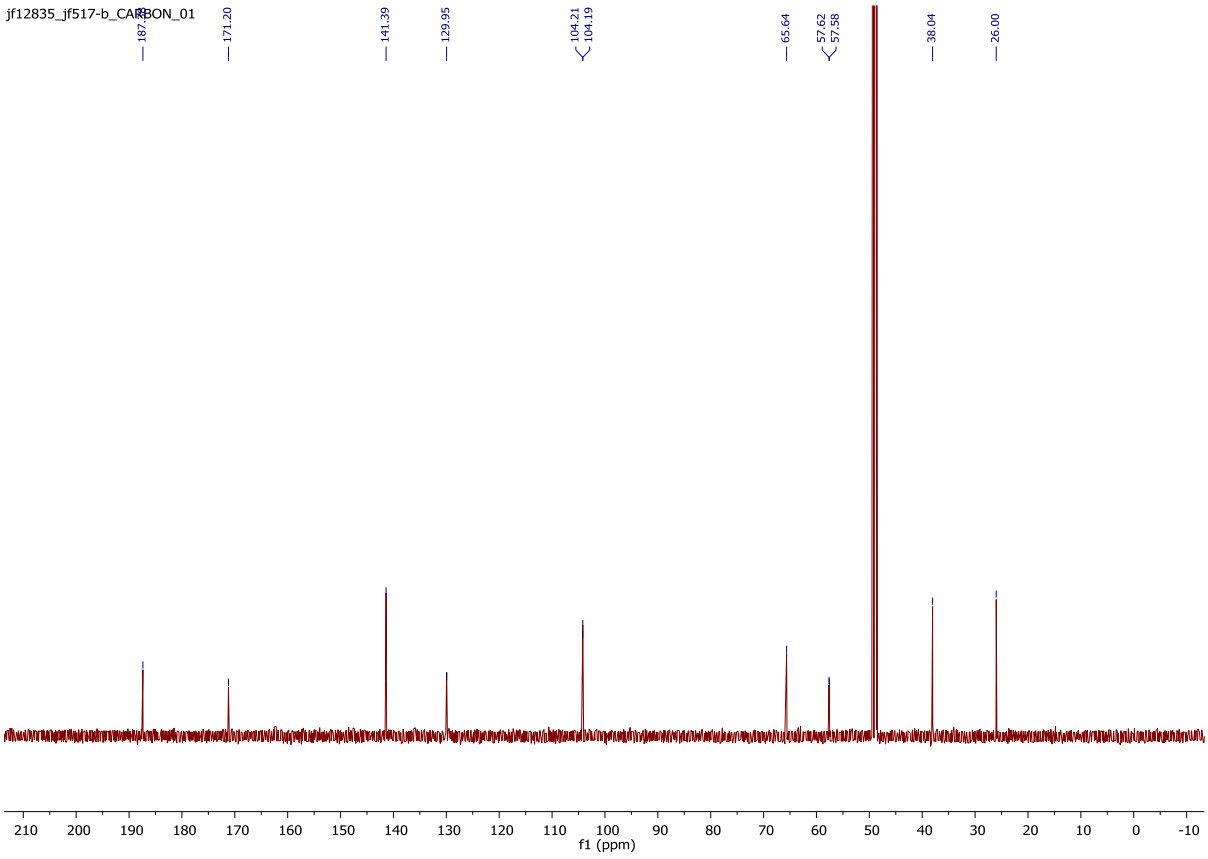
tert-Butyl (3-(4-hydroxy-2-methoxyphenyl)propyl)(tosyloxy)carbamate (5f)



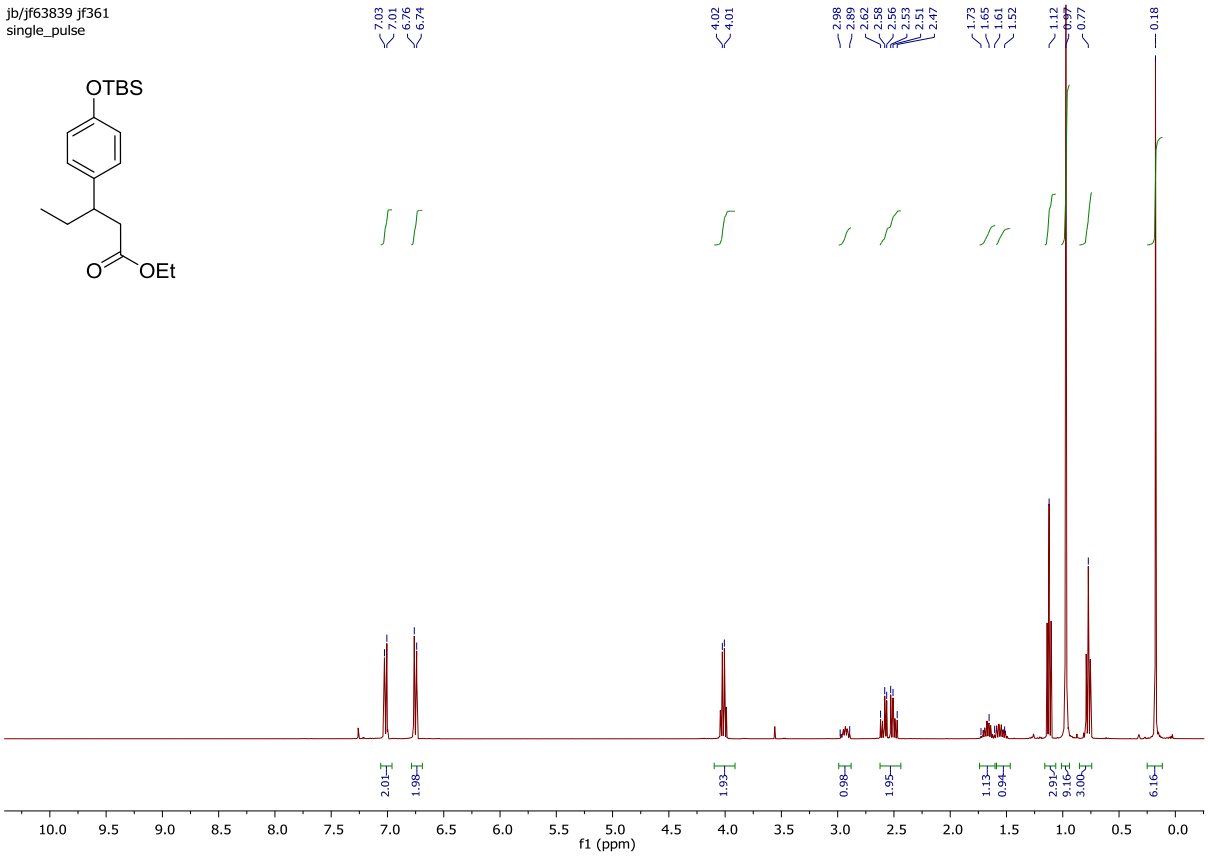


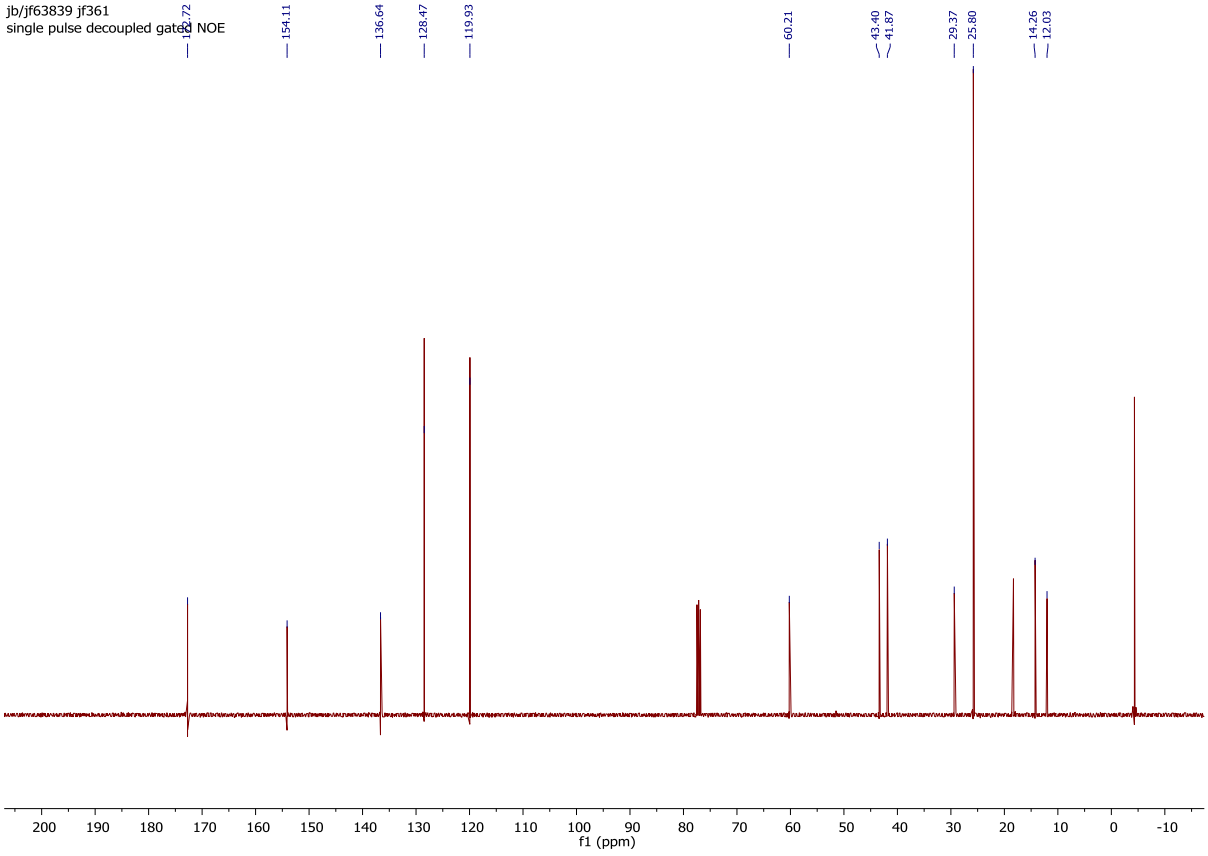
6-Methoxy-1-azaspiro[4.5]deca-6,9-dien-8-one trifluoroacetate (7f)



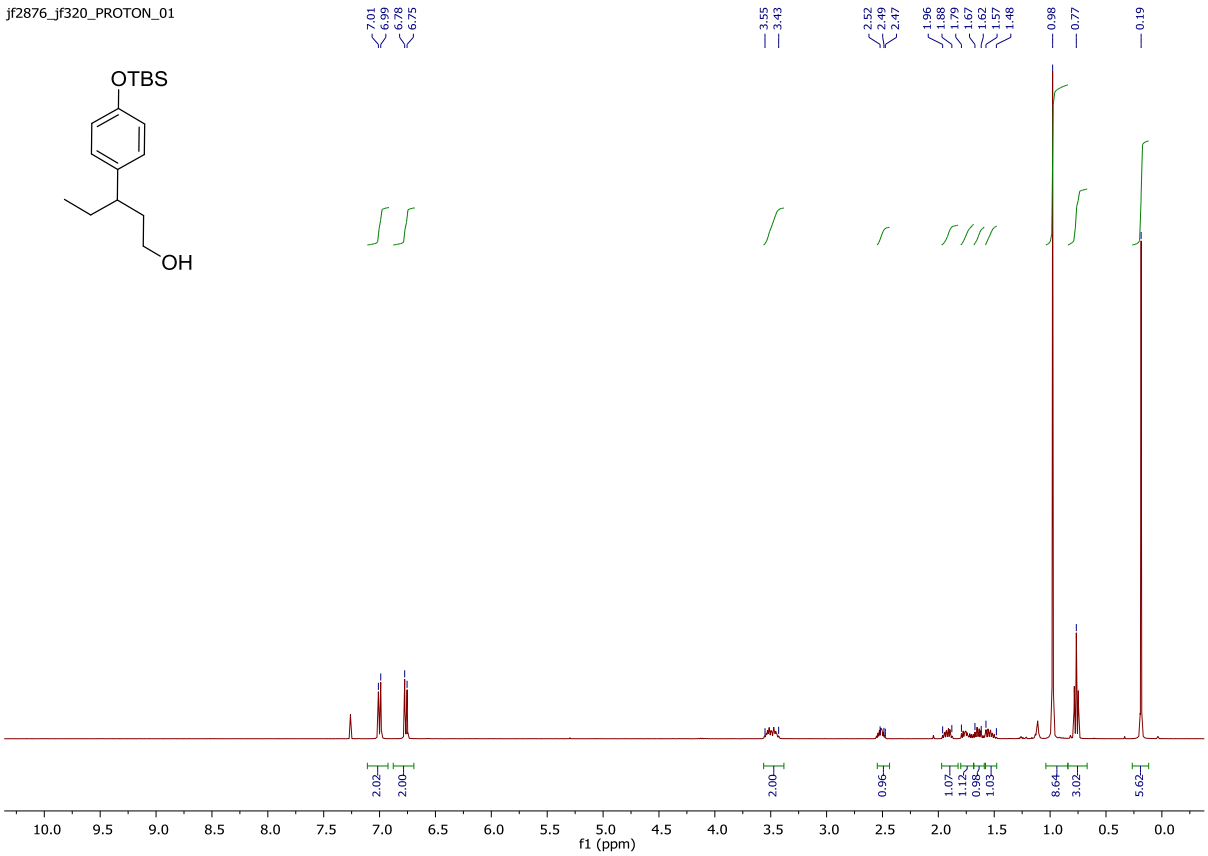


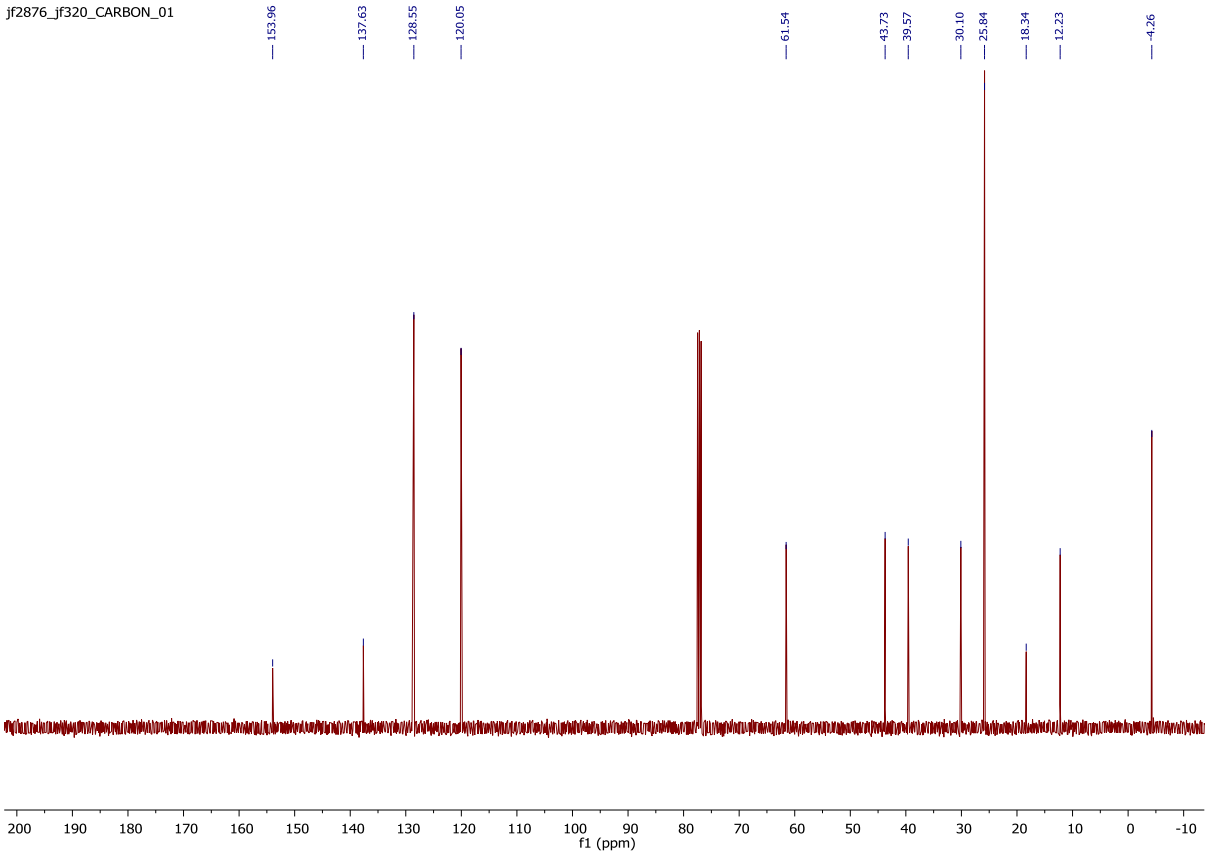
Ethyl 3-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)pentanoate



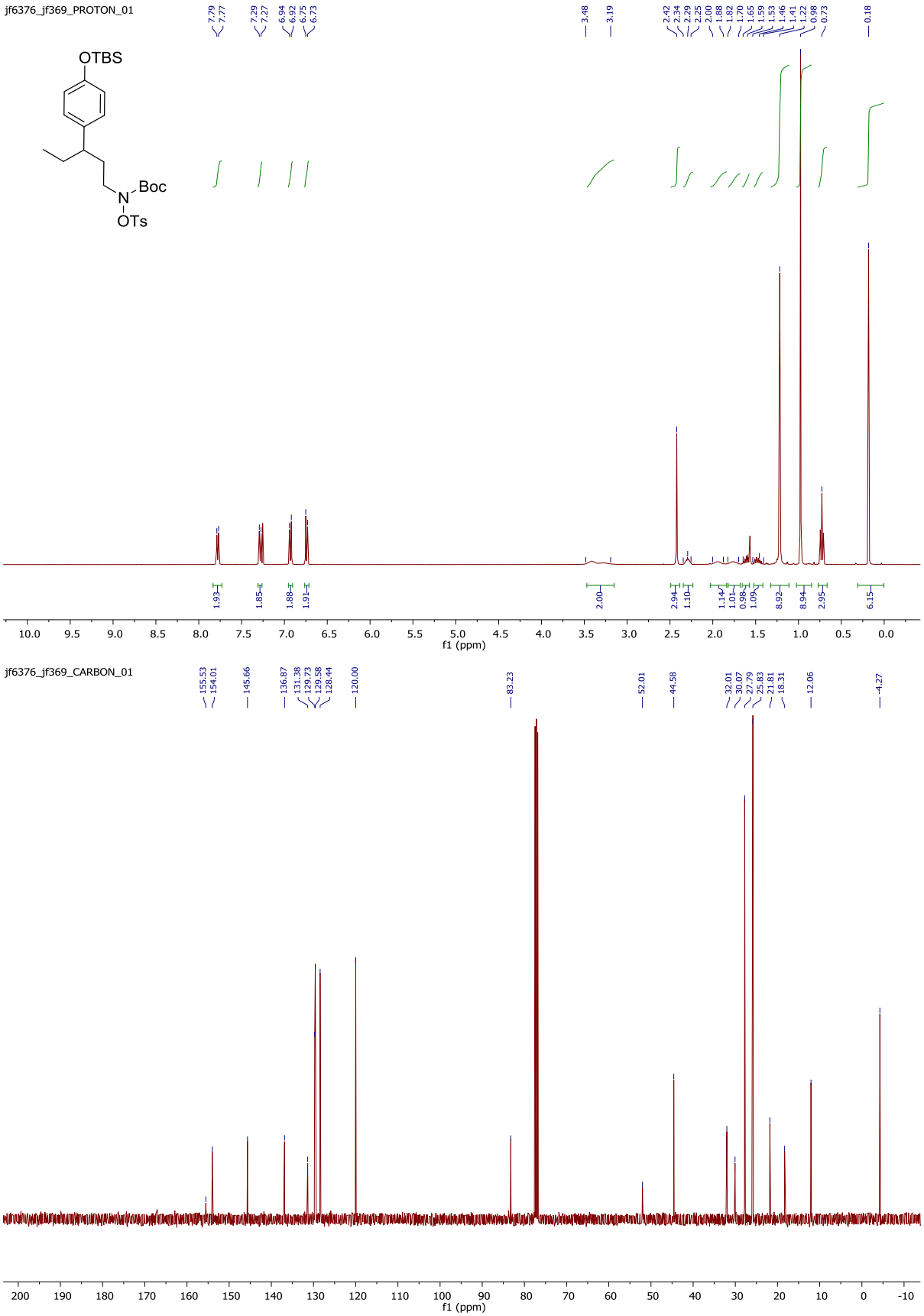


3-(4-((*tert*-Butyldimethylsilyl)oxy)phenyl)pentan-1-ol

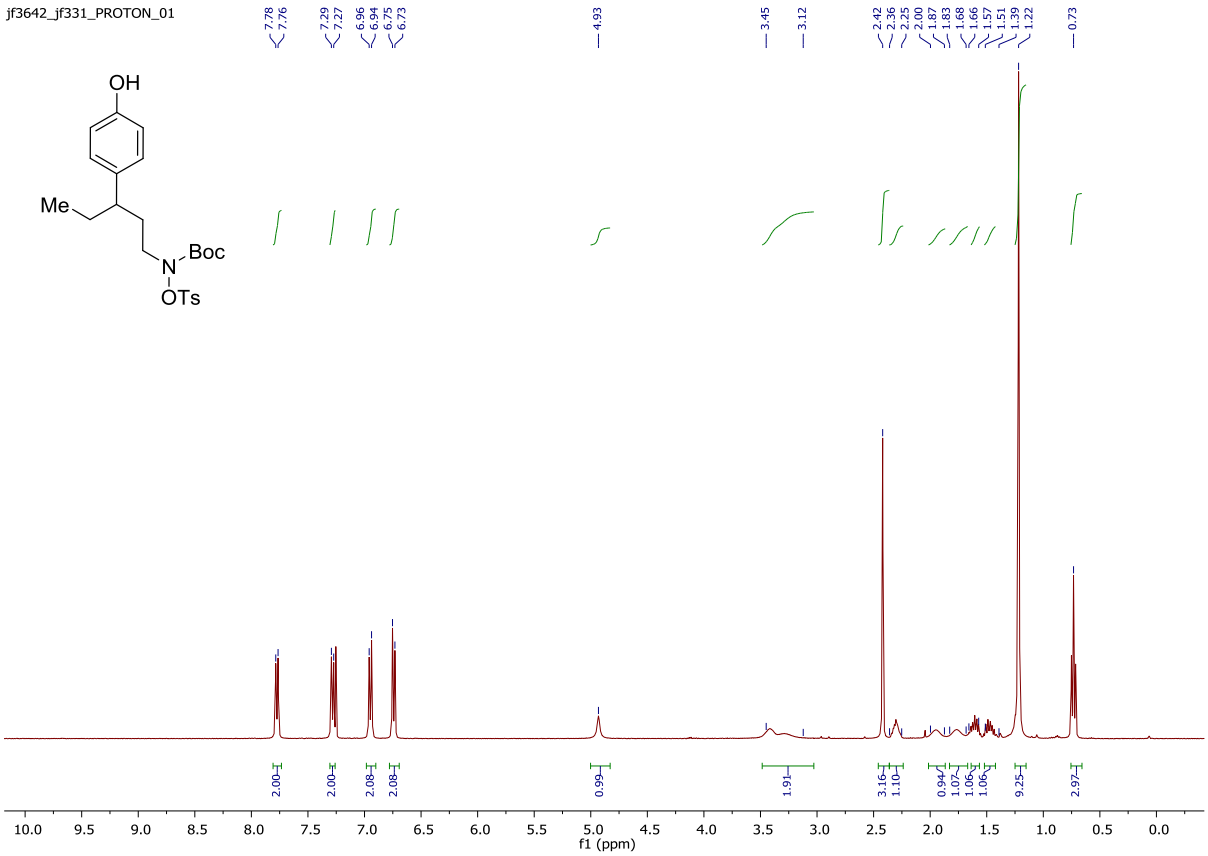


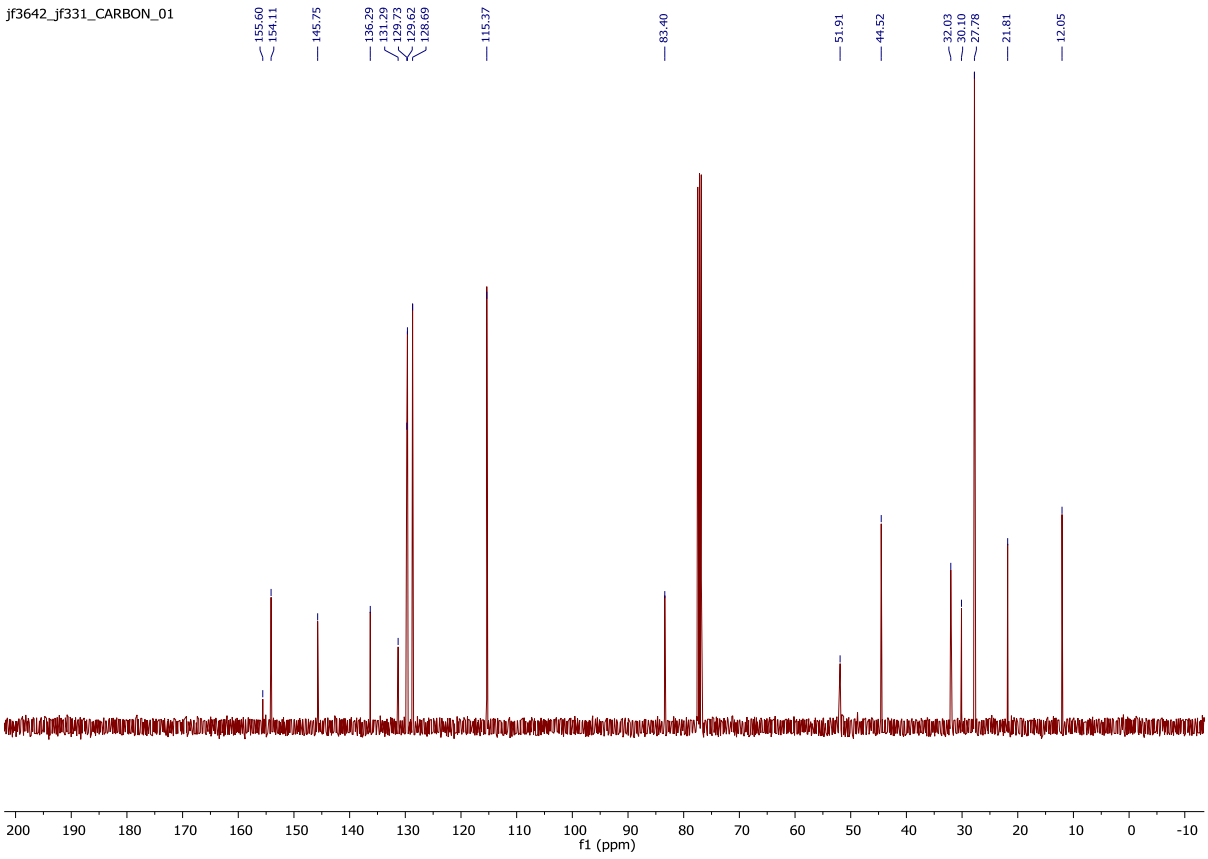


tert-Butyl (3-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)pentyl)(tosyloxy)carbamate

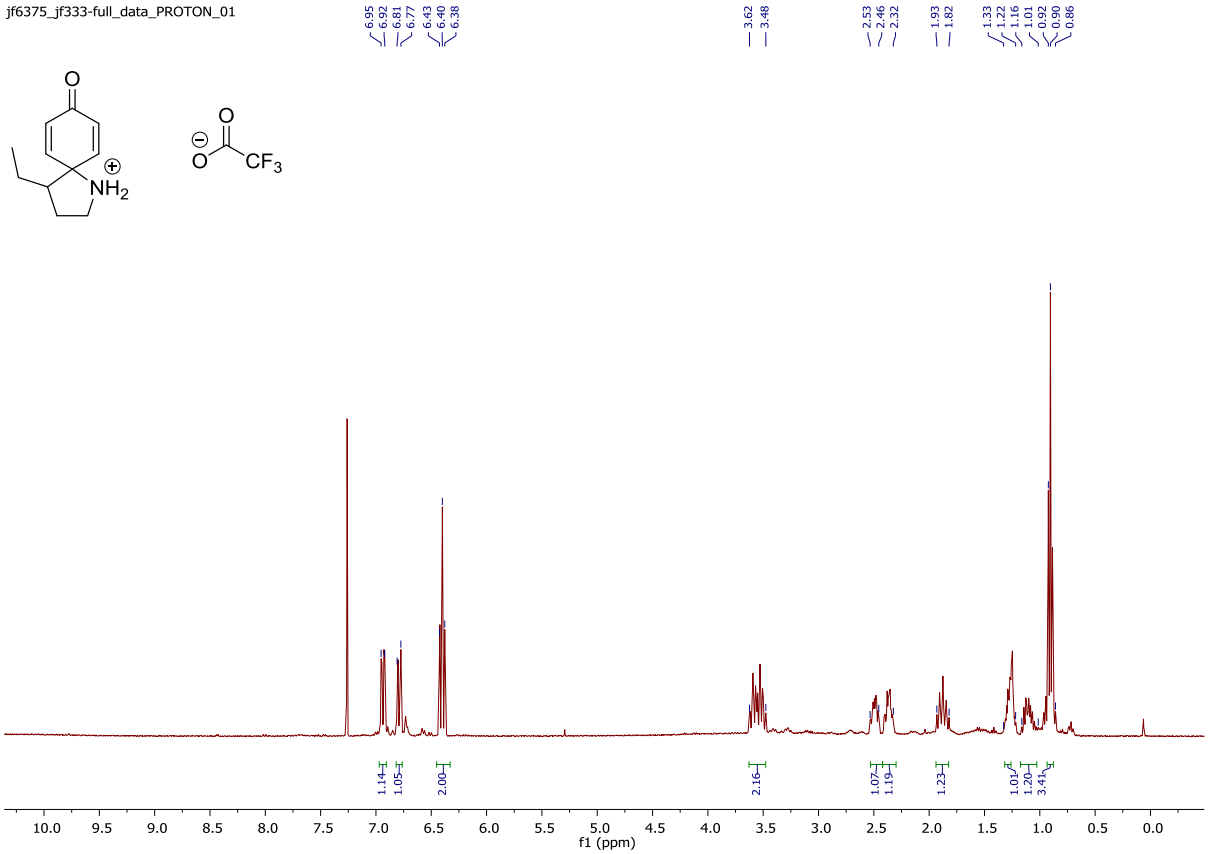


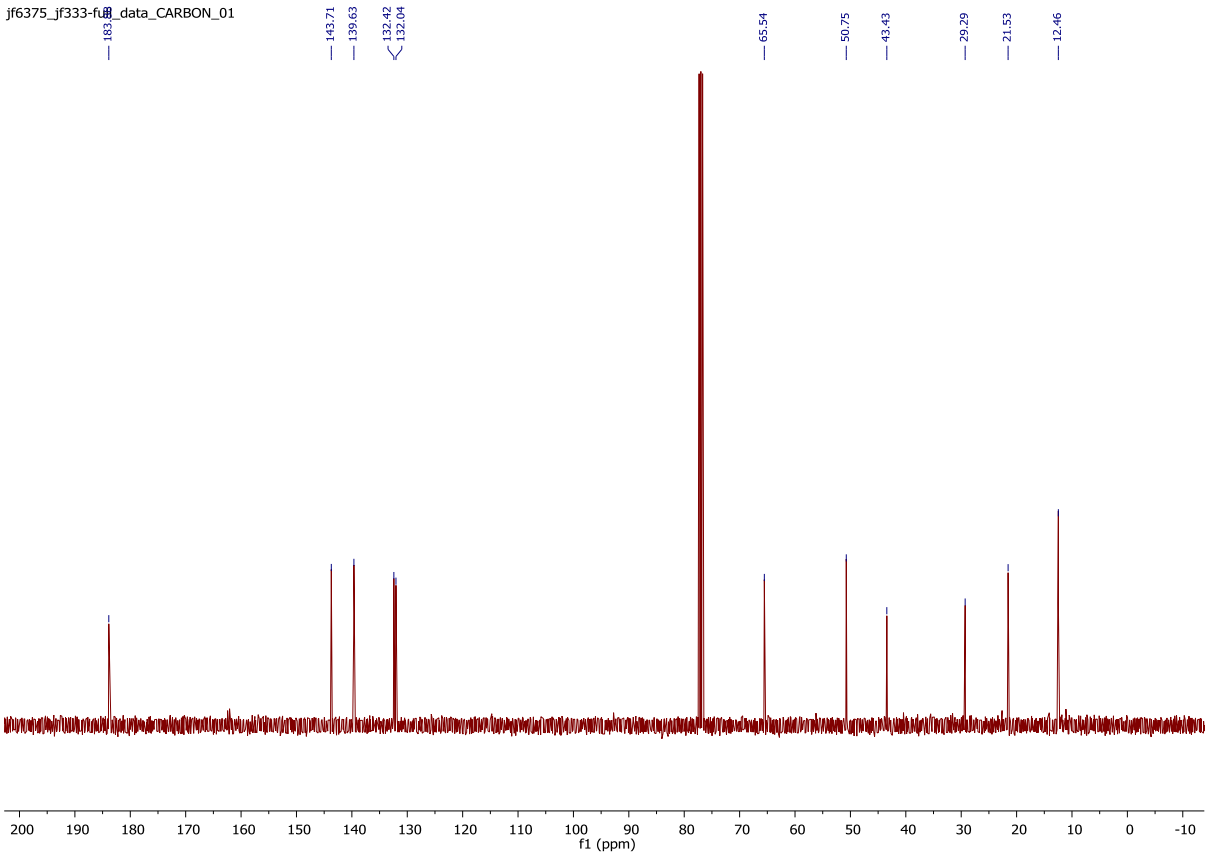
tert-Butyl (3-(4-hydroxyphenyl)pentyl)(tosyloxy)carbamate (5g)



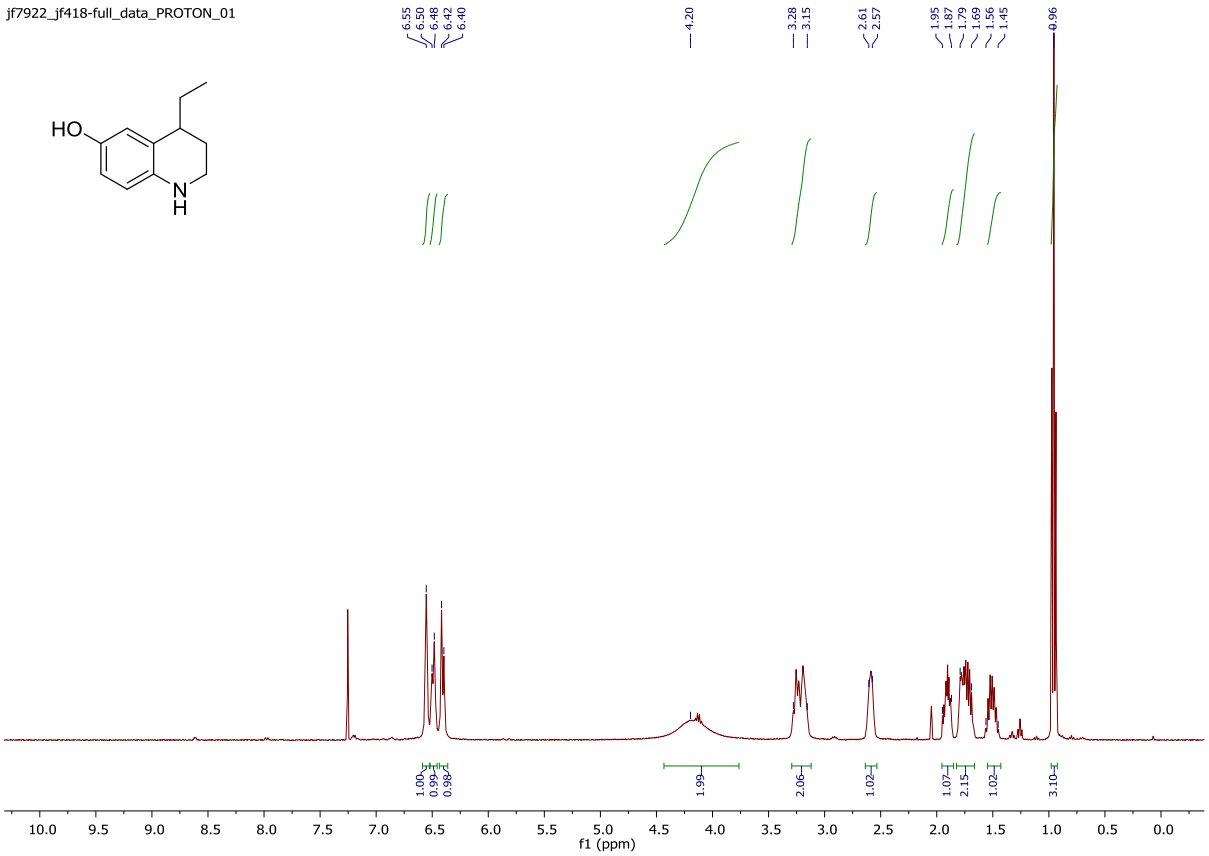


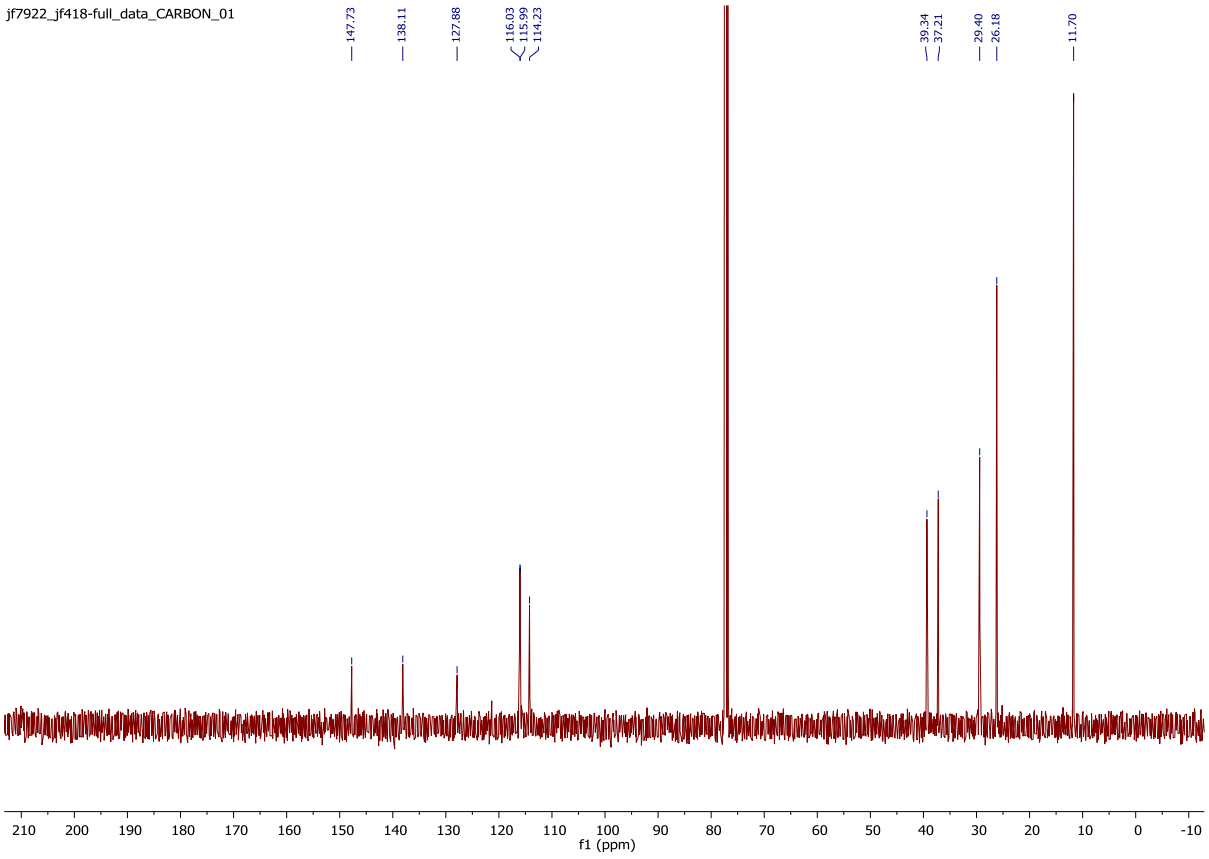
4-Ethyl-1-azaspiro[4.5]deca-6,9-dien-8-one trifluoroacetate (7g)



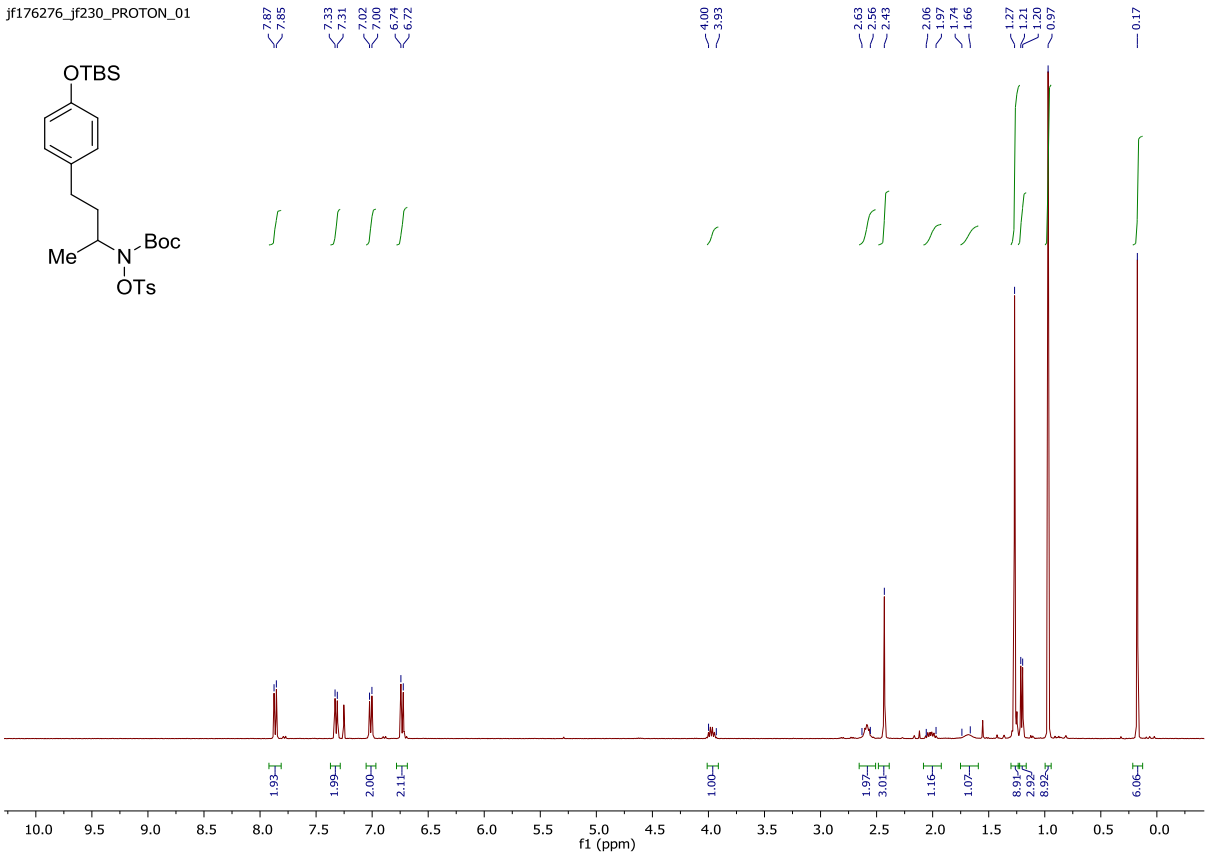


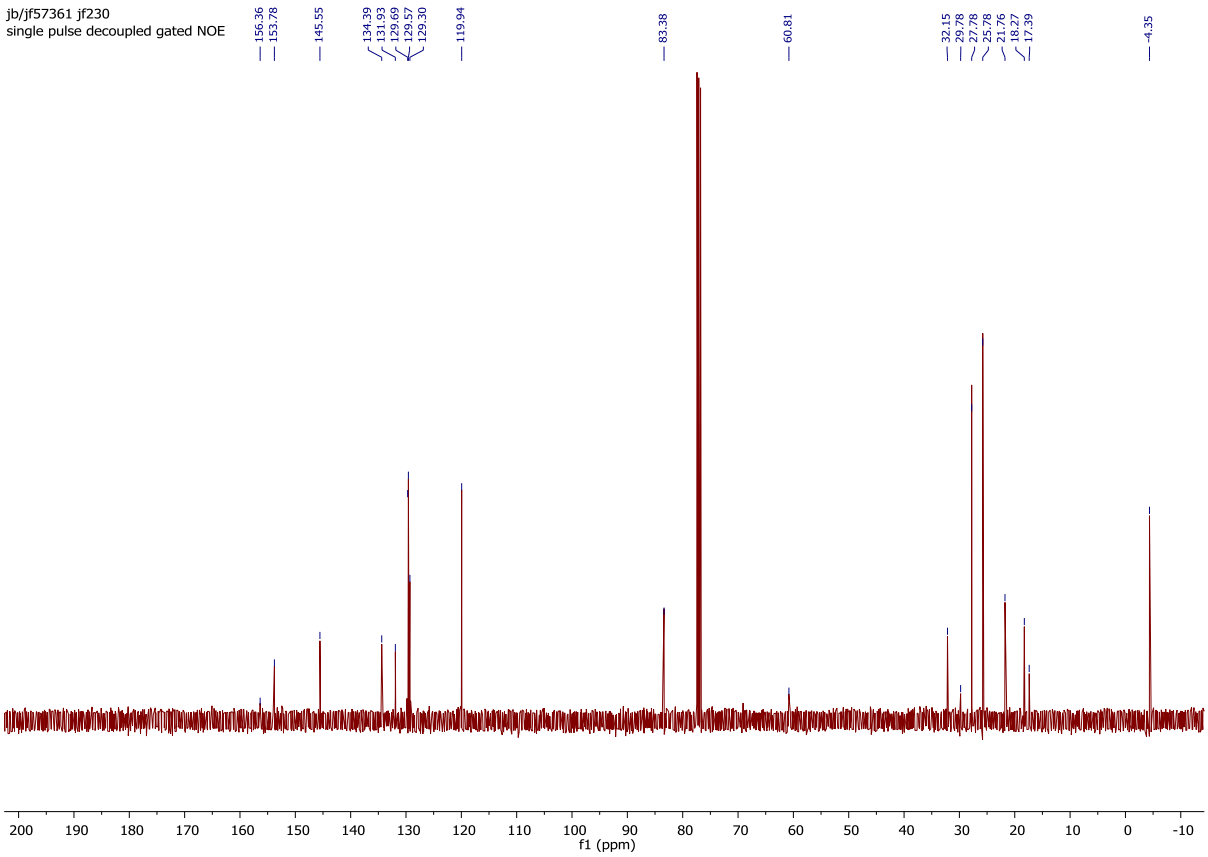
4-Ethyl-1,2,3,4-tetrahydroquinolin-7-ol (8g)



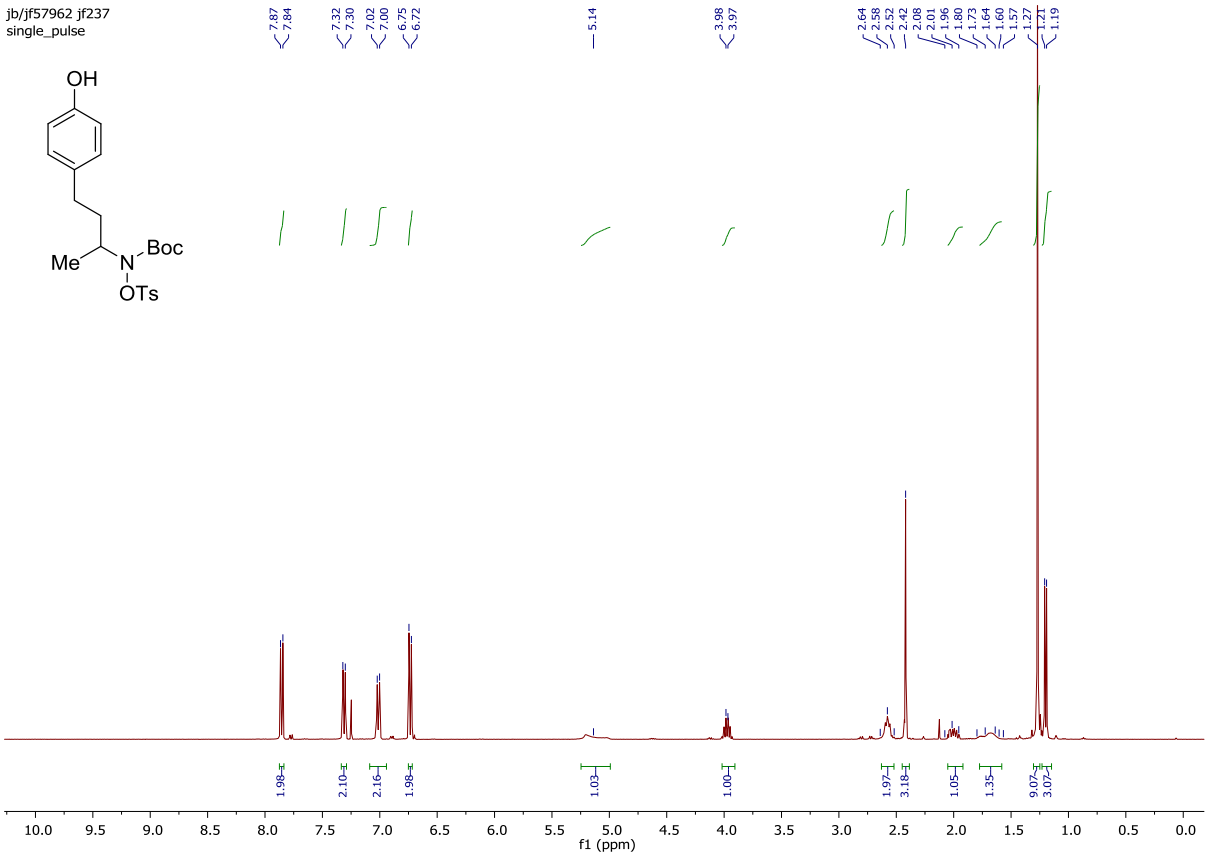


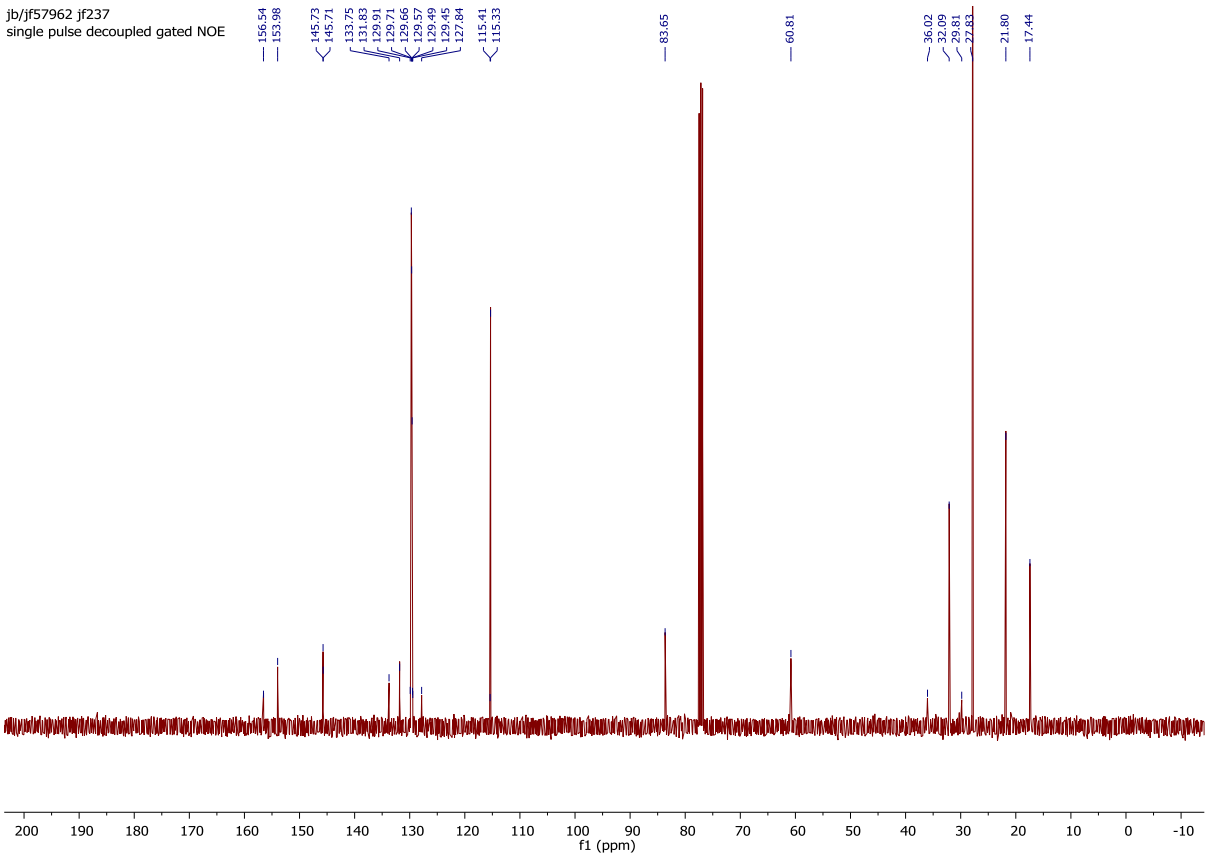
tert-Butyl (4-(4-((_tert_-butyldimethylsilyl)oxy)phenyl)butan-2-yl)(tosyloxy)carbamate



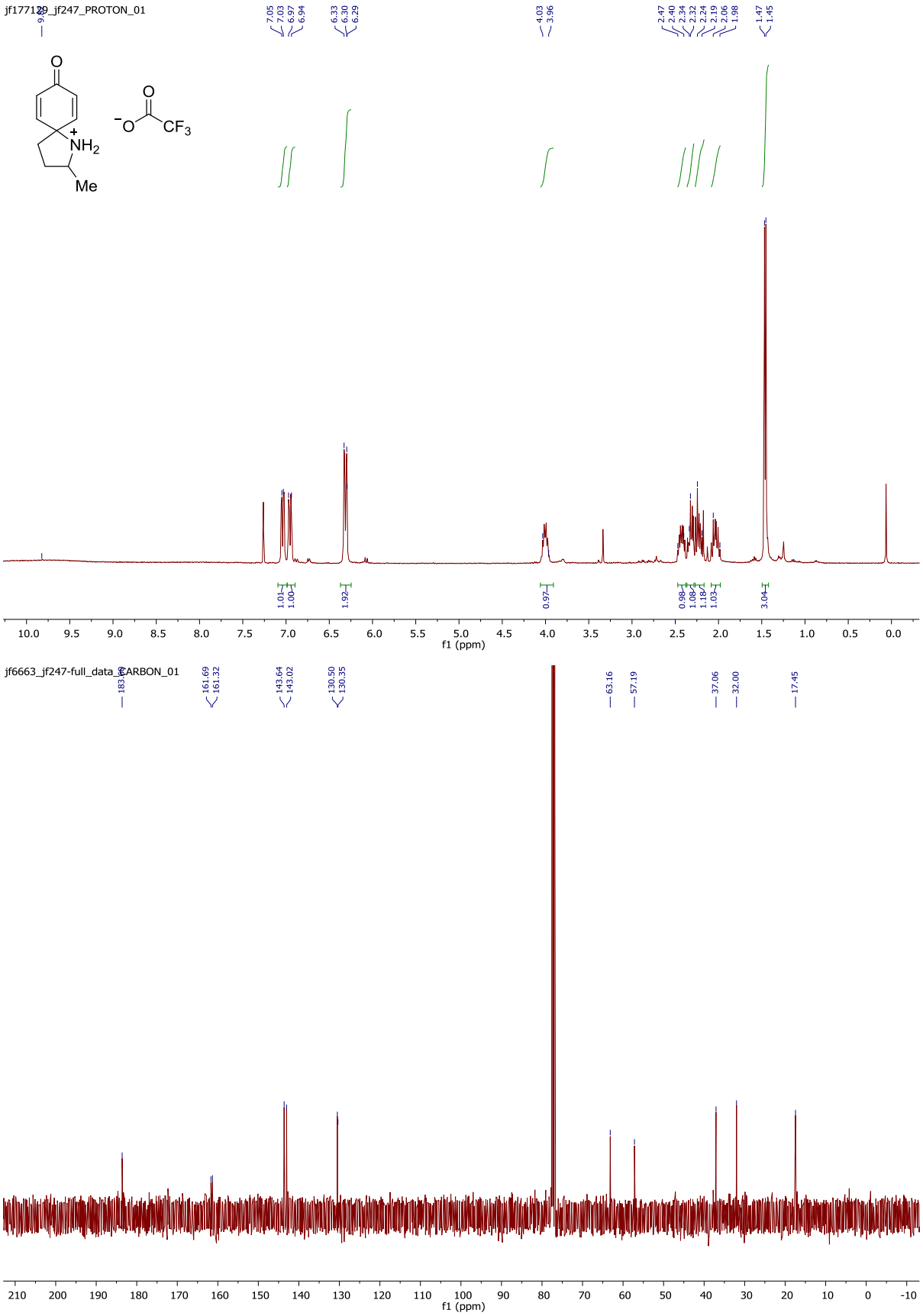


tert-Butyl (4-(4-hydroxyphenyl)butan-2-yl)(tosyloxy)carbamate (5h)

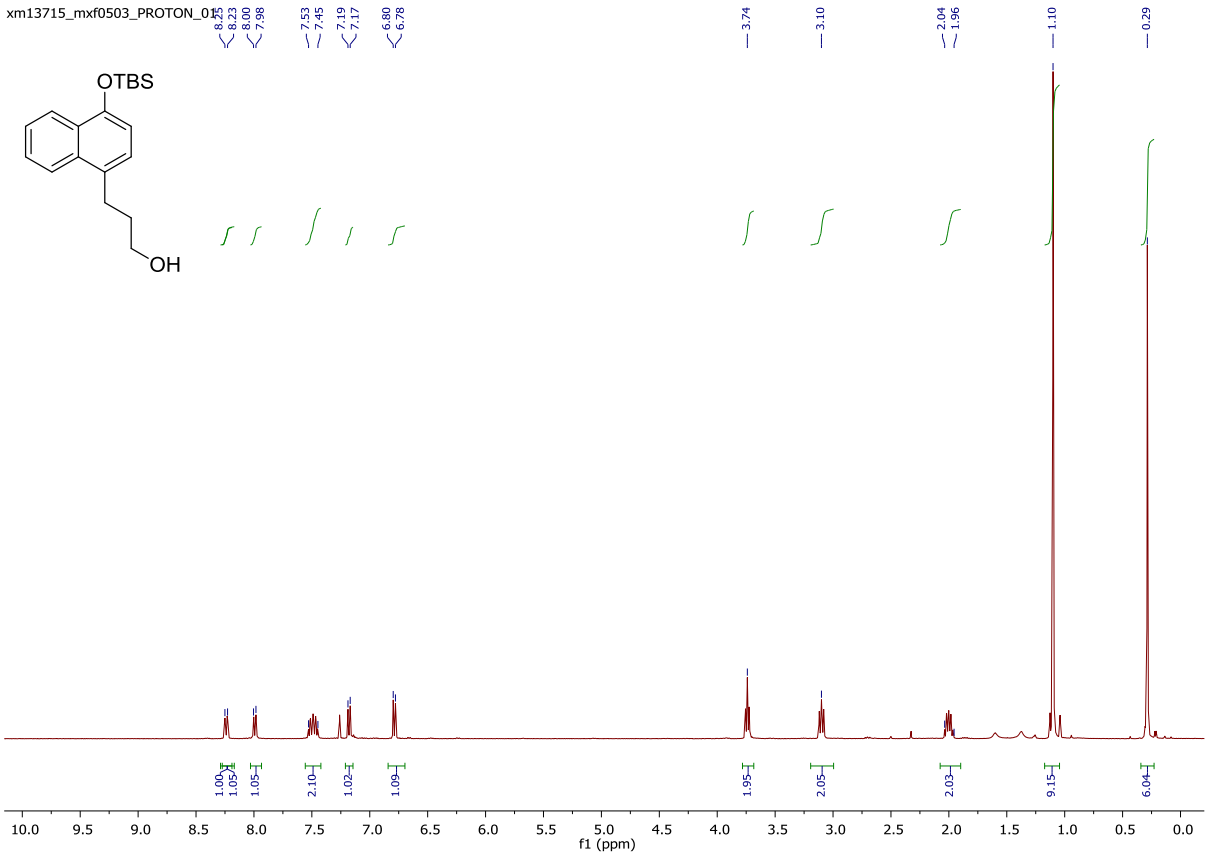


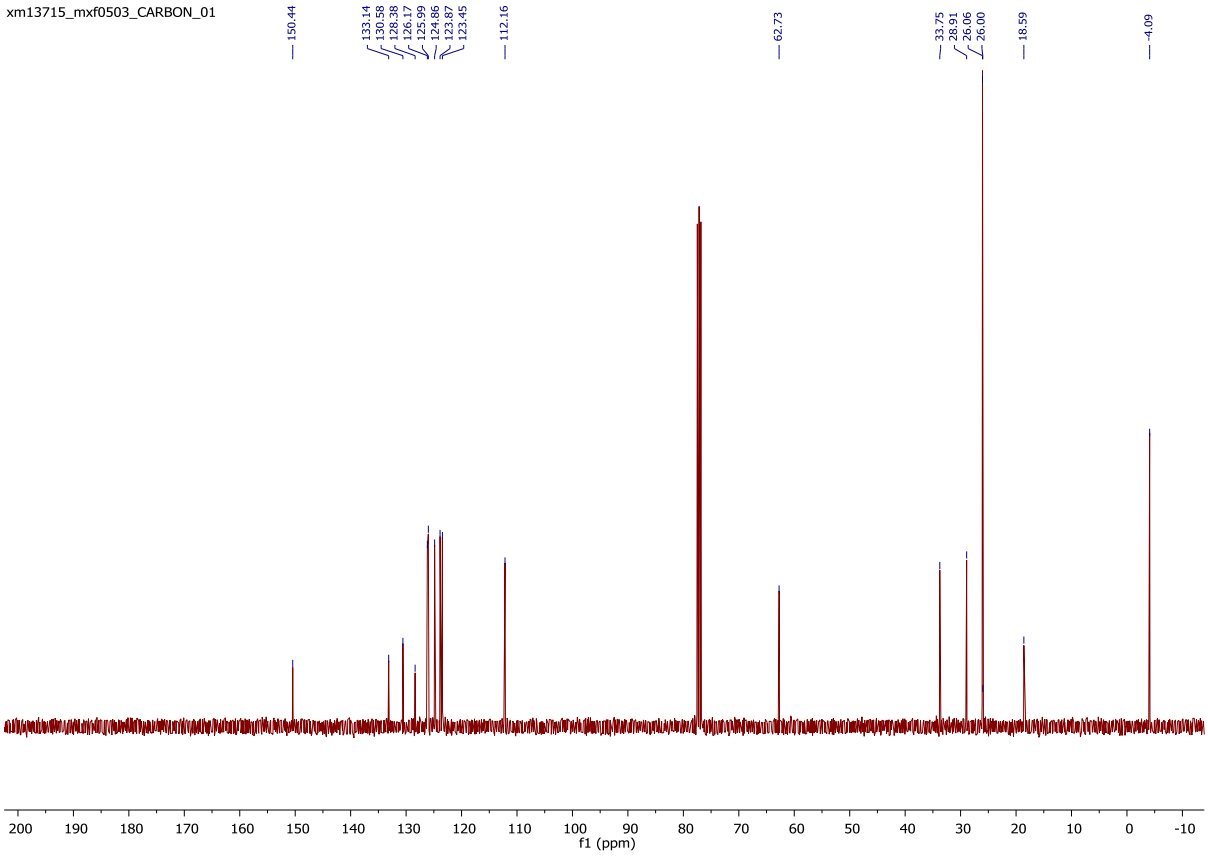


2-Methyl-1-azaspiro[4.5]deca-6,9-dien-8-one trifluoroacetate (7h)

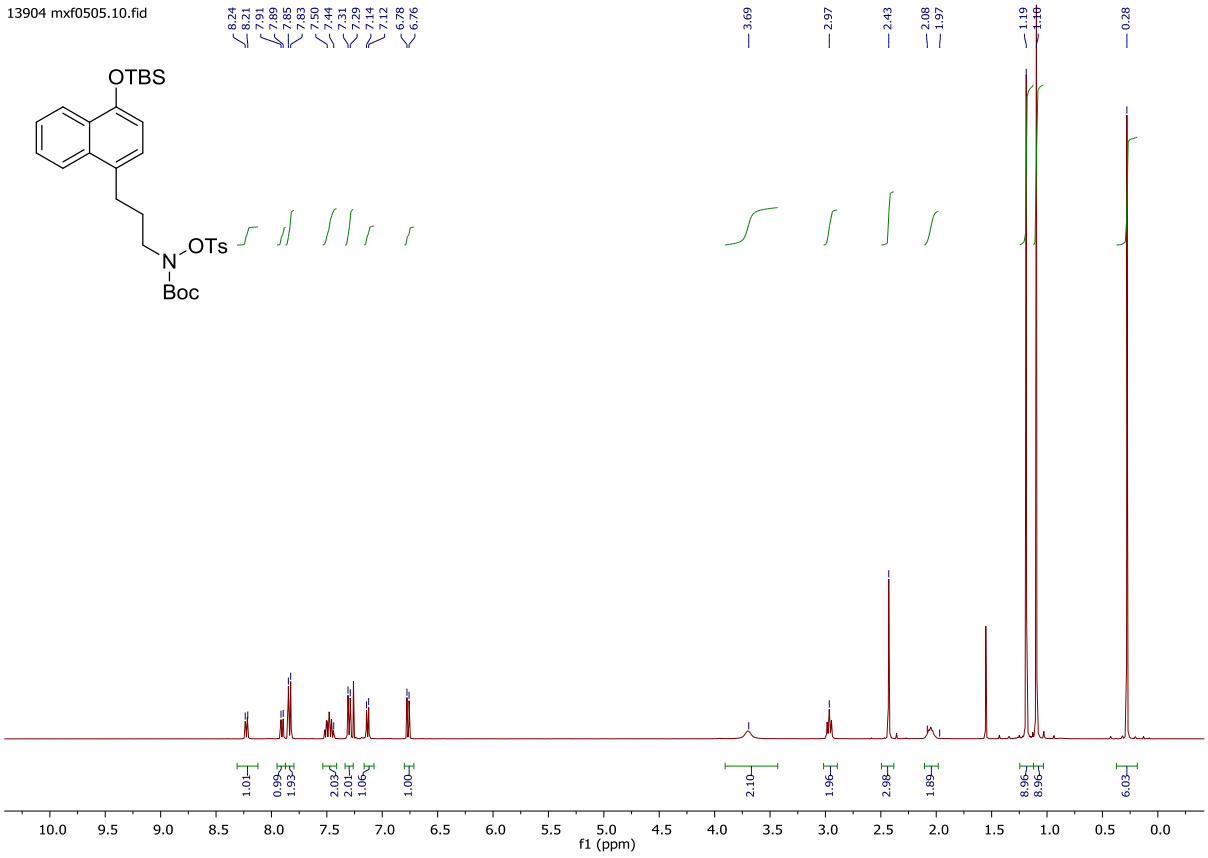


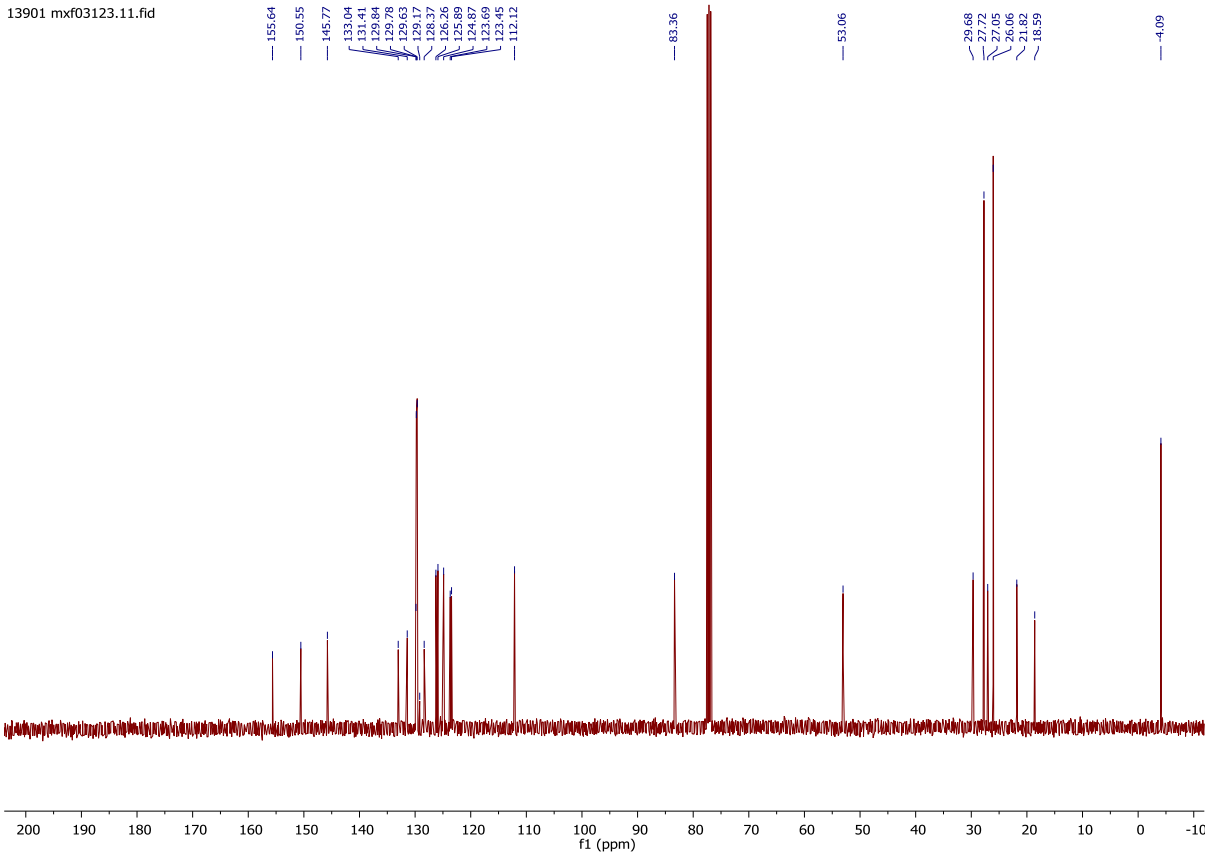
3-(4-((*tert*-Butyldimethylsilyl)oxy)naphthalen-1-yl)propan-1-ol



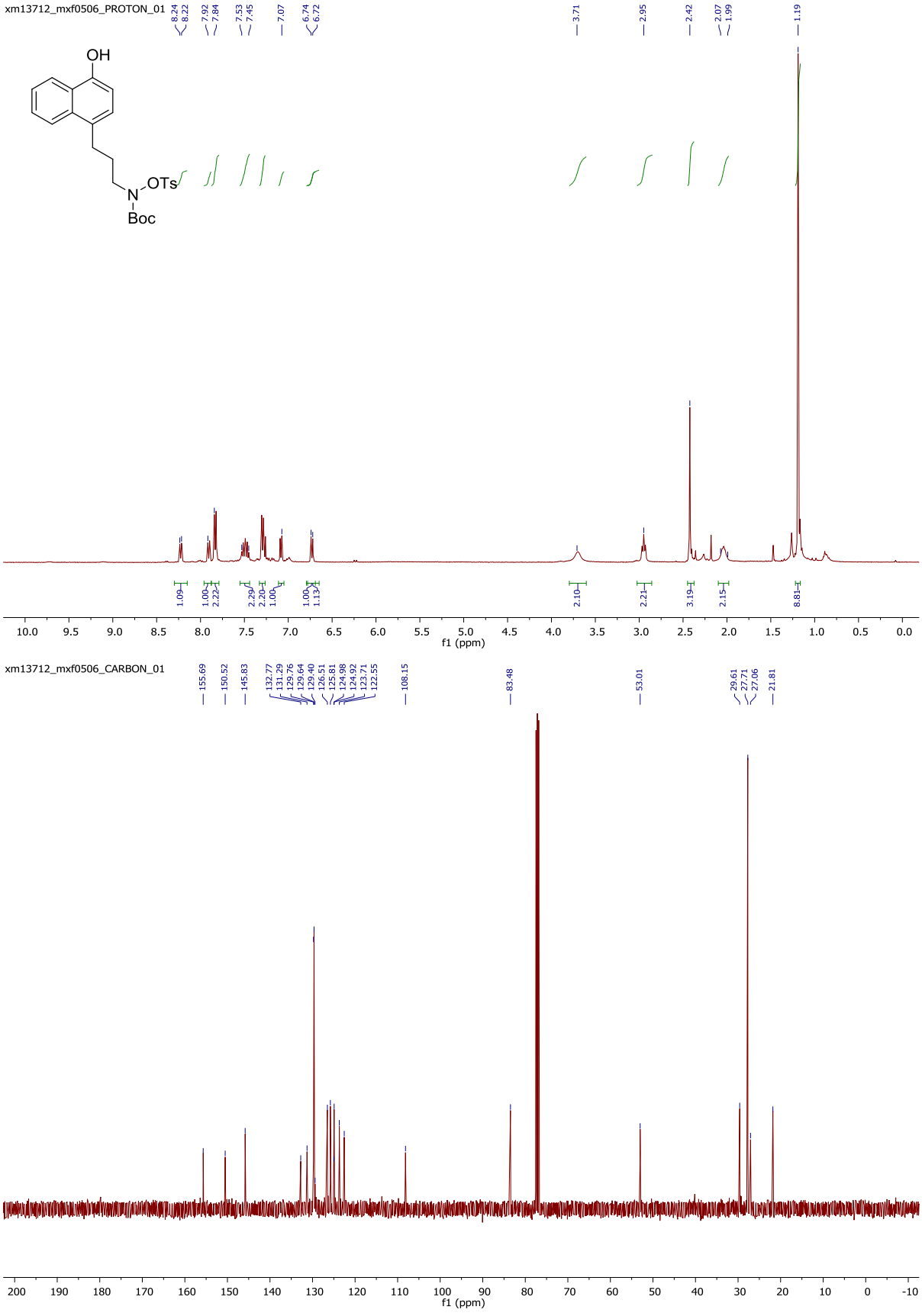


tert-Butyl (3-(4-((_tert_-butyldimethylsilyl)oxy)naphthalen-1-yl)propyl)(tosyloxy)carbamate

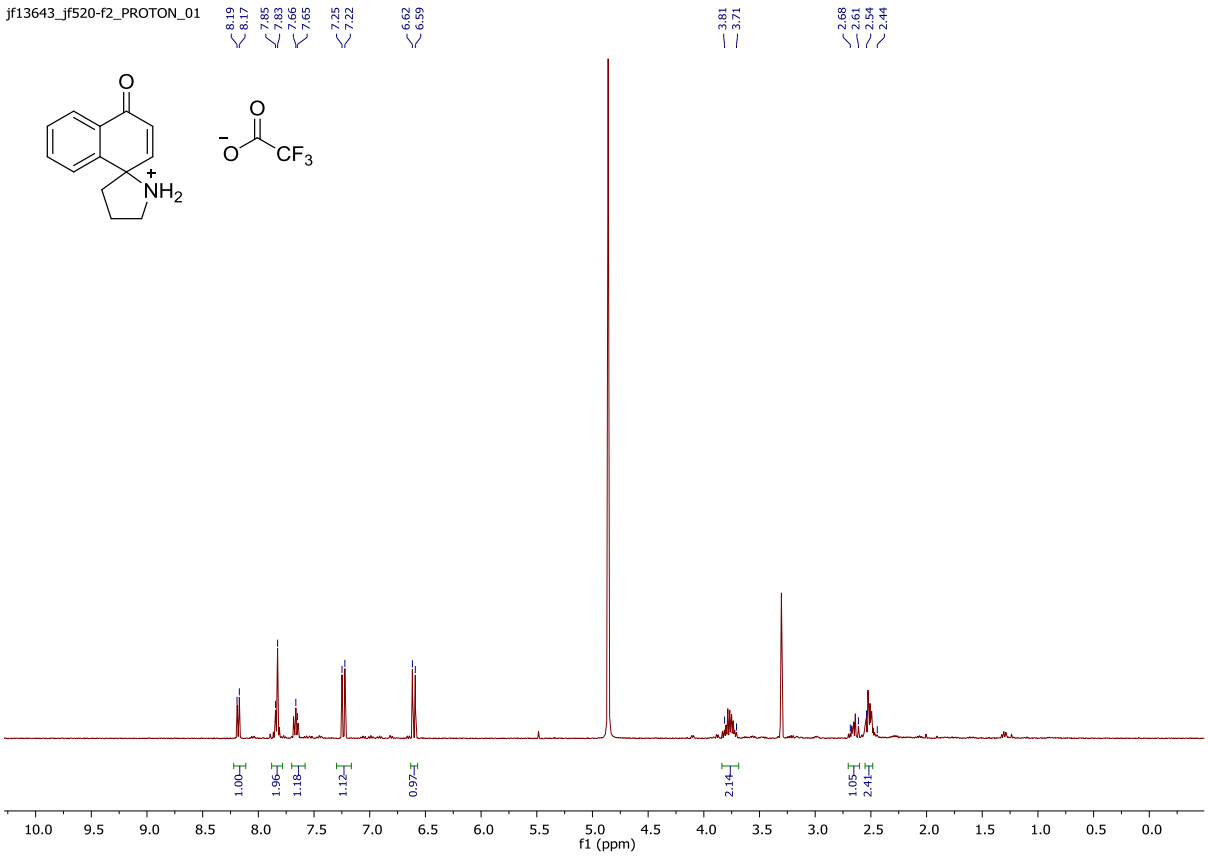


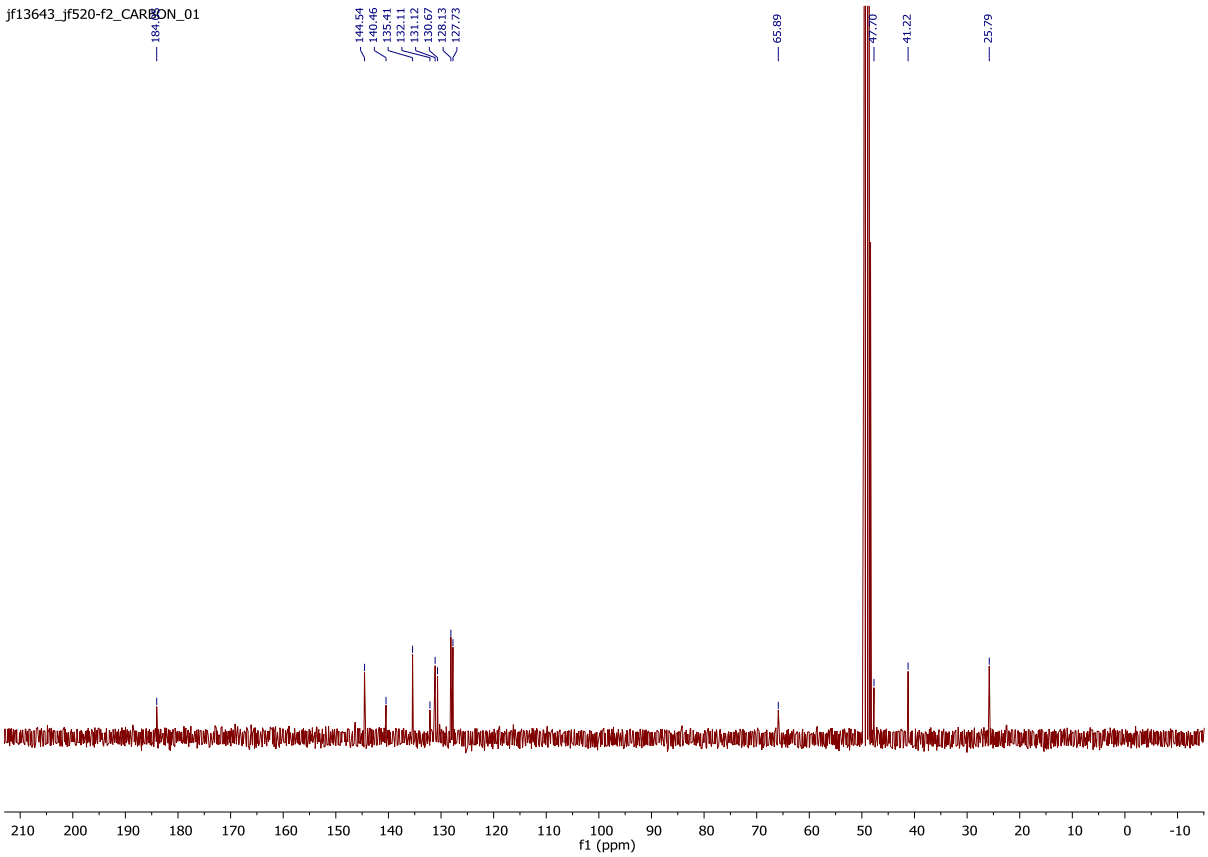


tert-Butyl (3-(4-hydroxynaphthalen-1-yl)propyl)(tosyloxy)carbamate (5i)

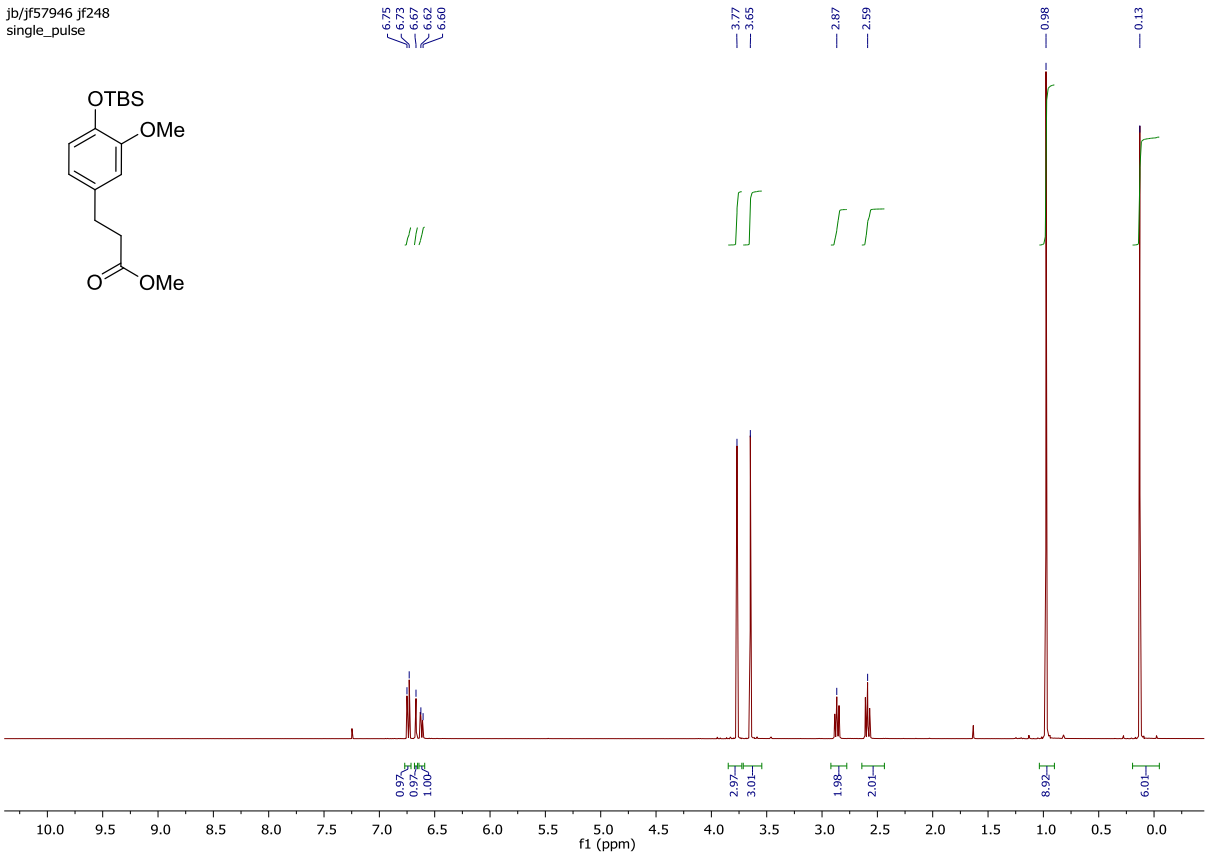


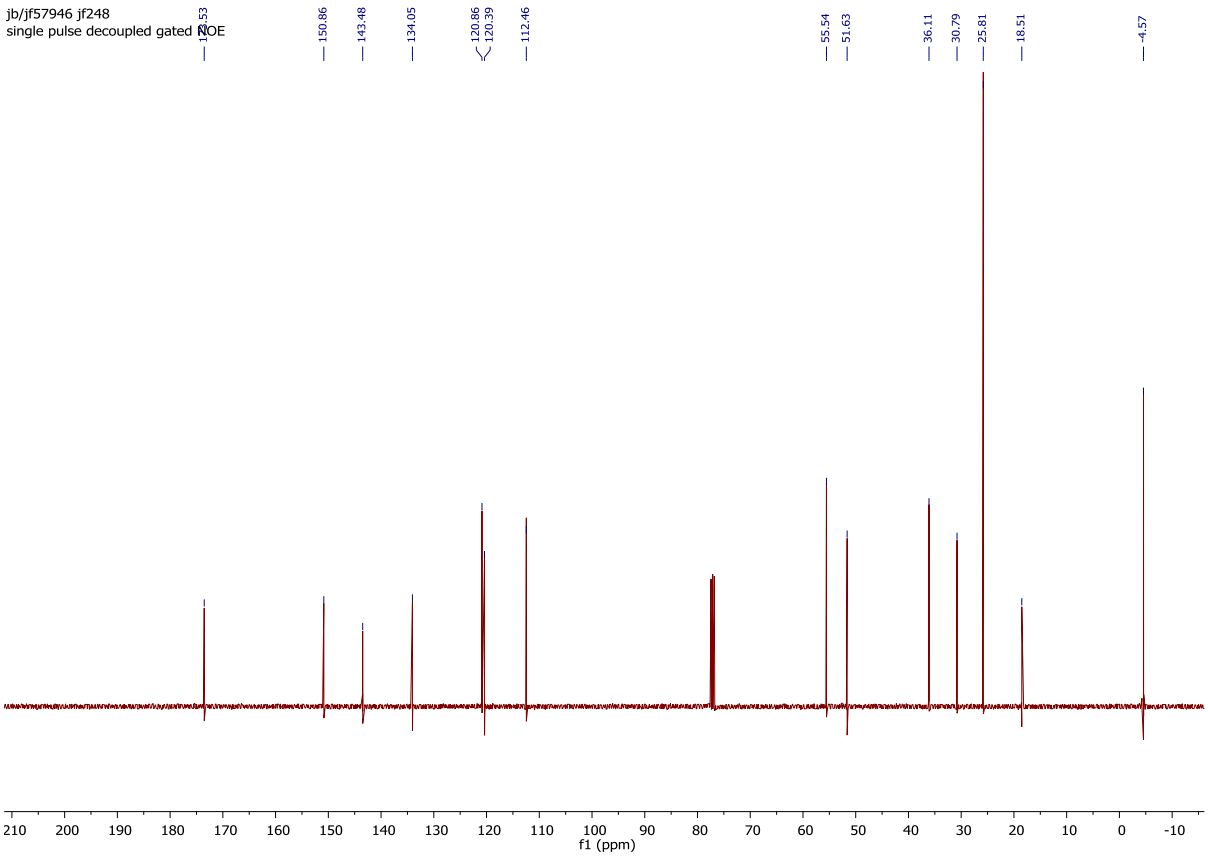
4H-spiro[naphthalene-1,2'-pyrrolidin]-4-one trifluoroacetate (7i)



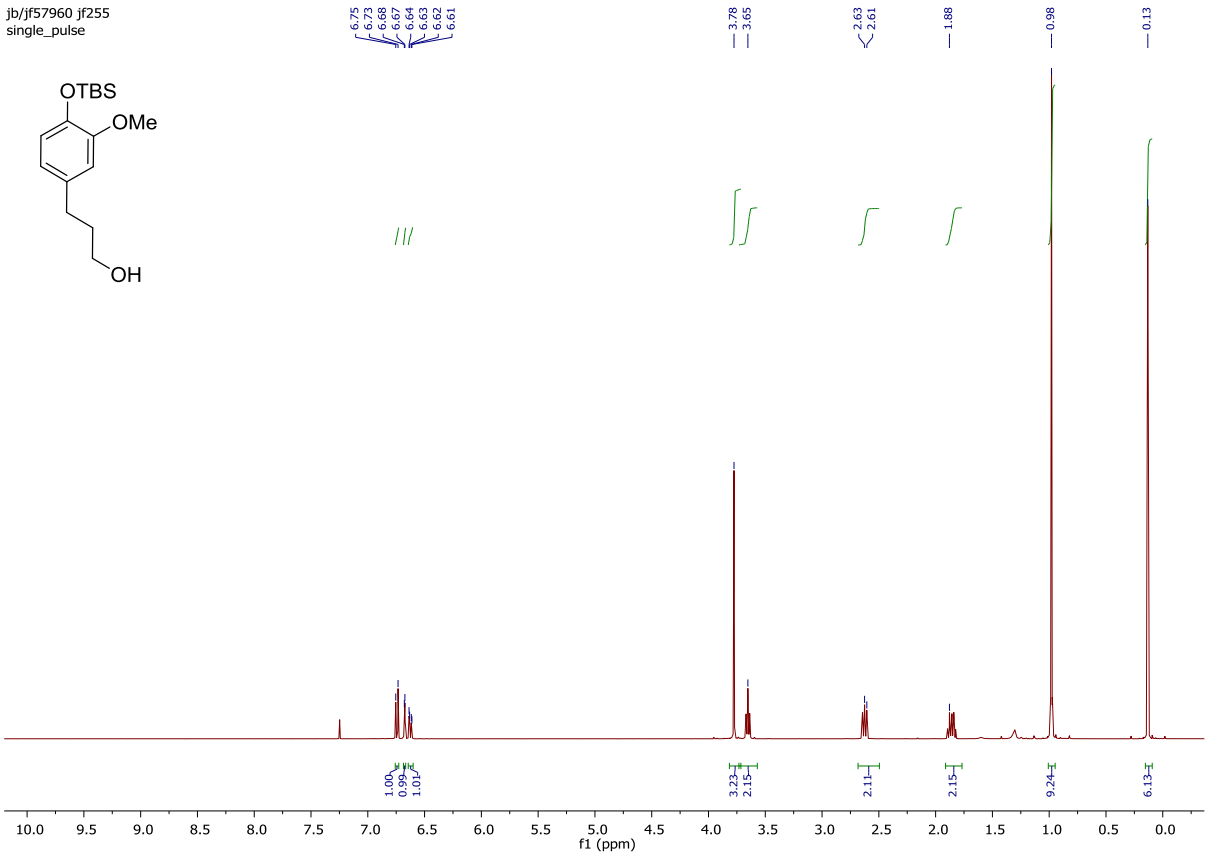


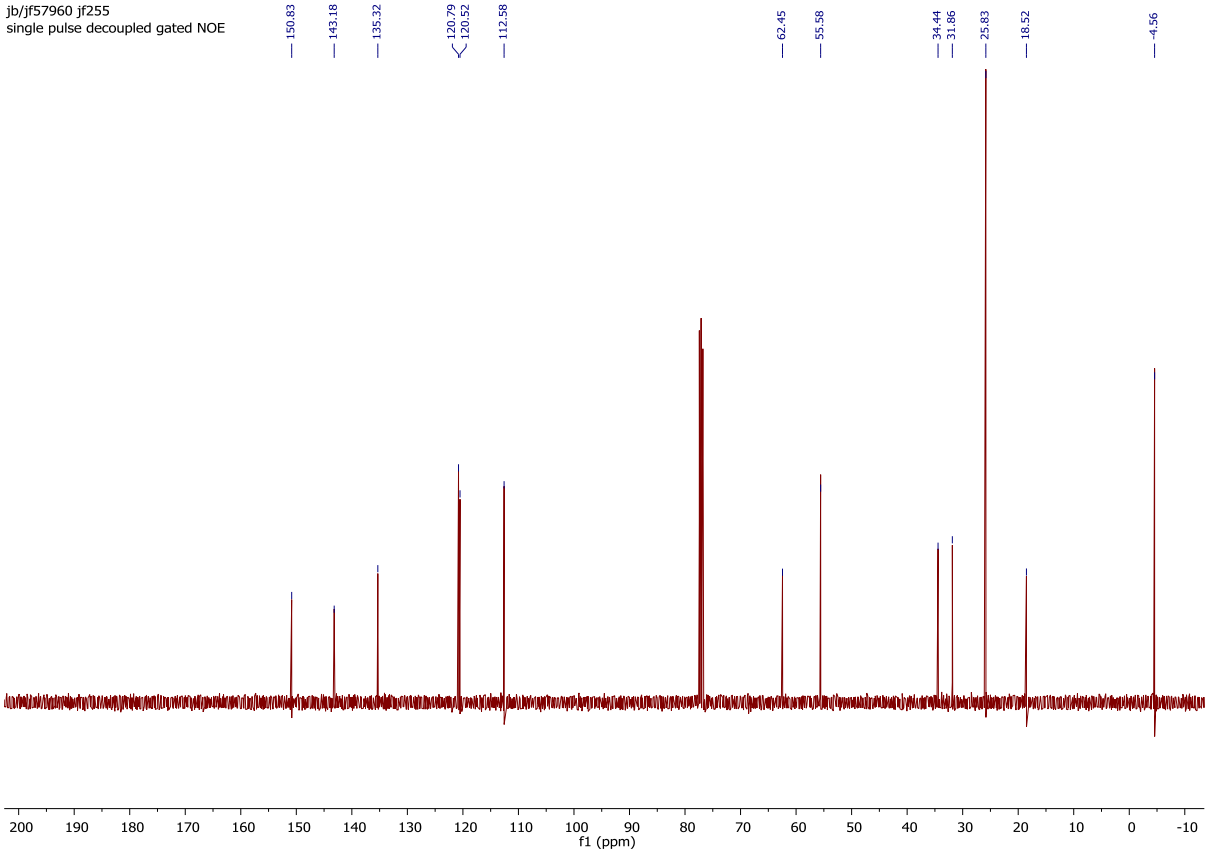
Methyl 3-(4-((*tert*-butyldimethylsilyl)oxy)-3-methoxyphenyl)propanoate



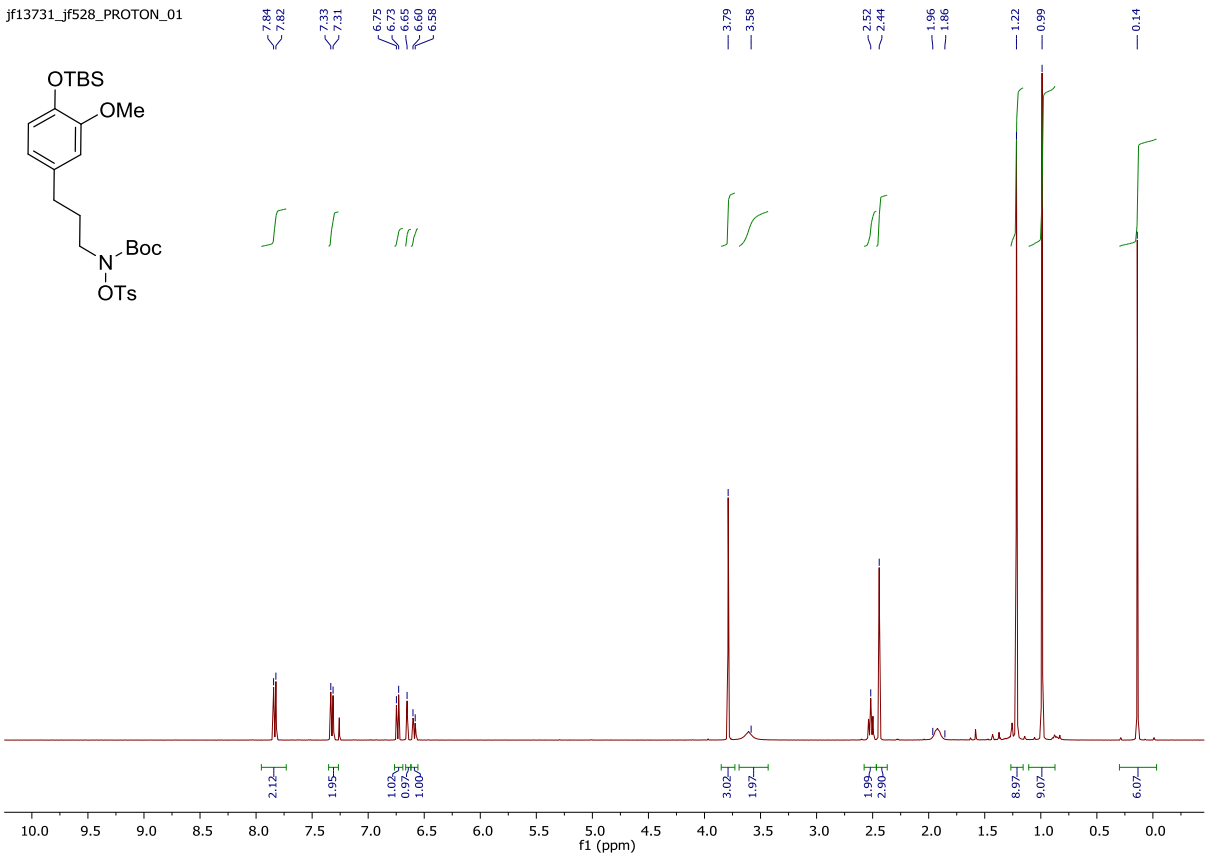


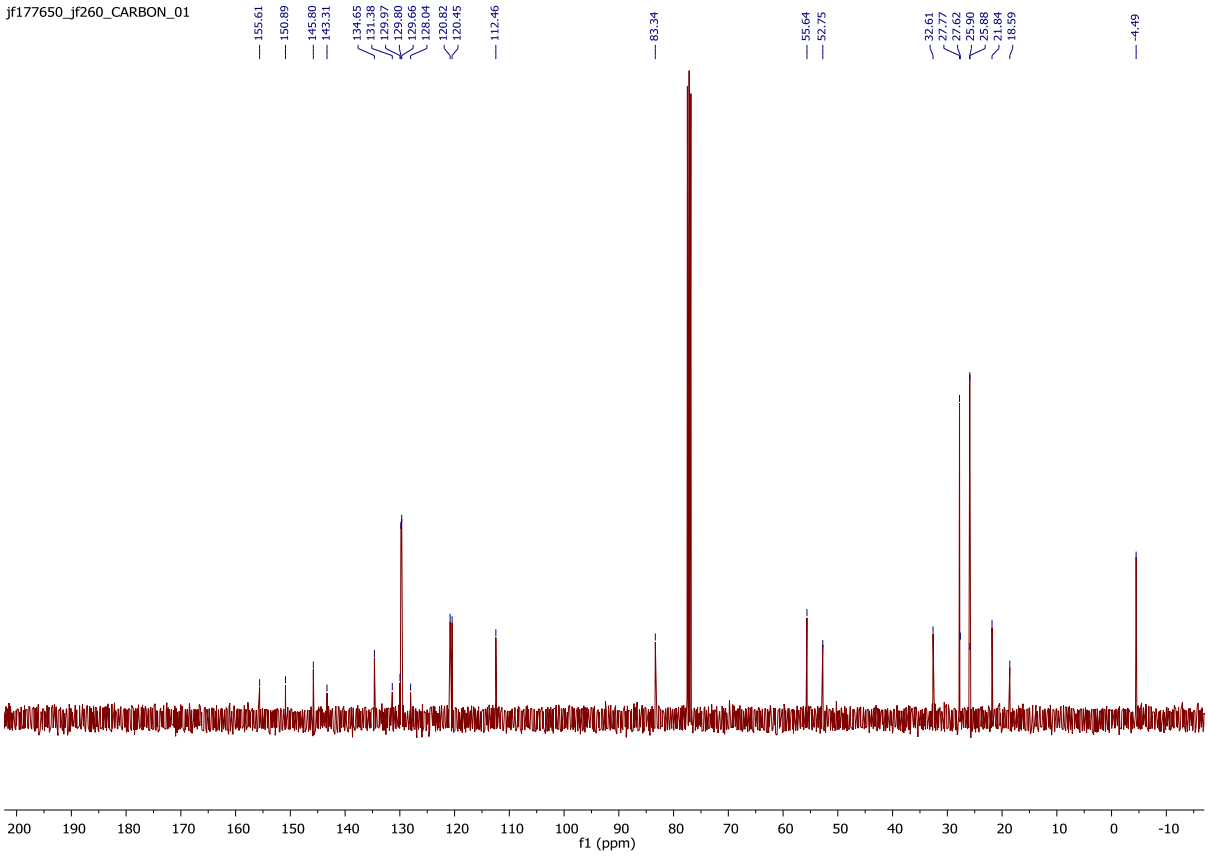
3-(4-((*tert*-Butyldimethylsilyl)oxy)-3-methoxyphenyl)propan-1-ol



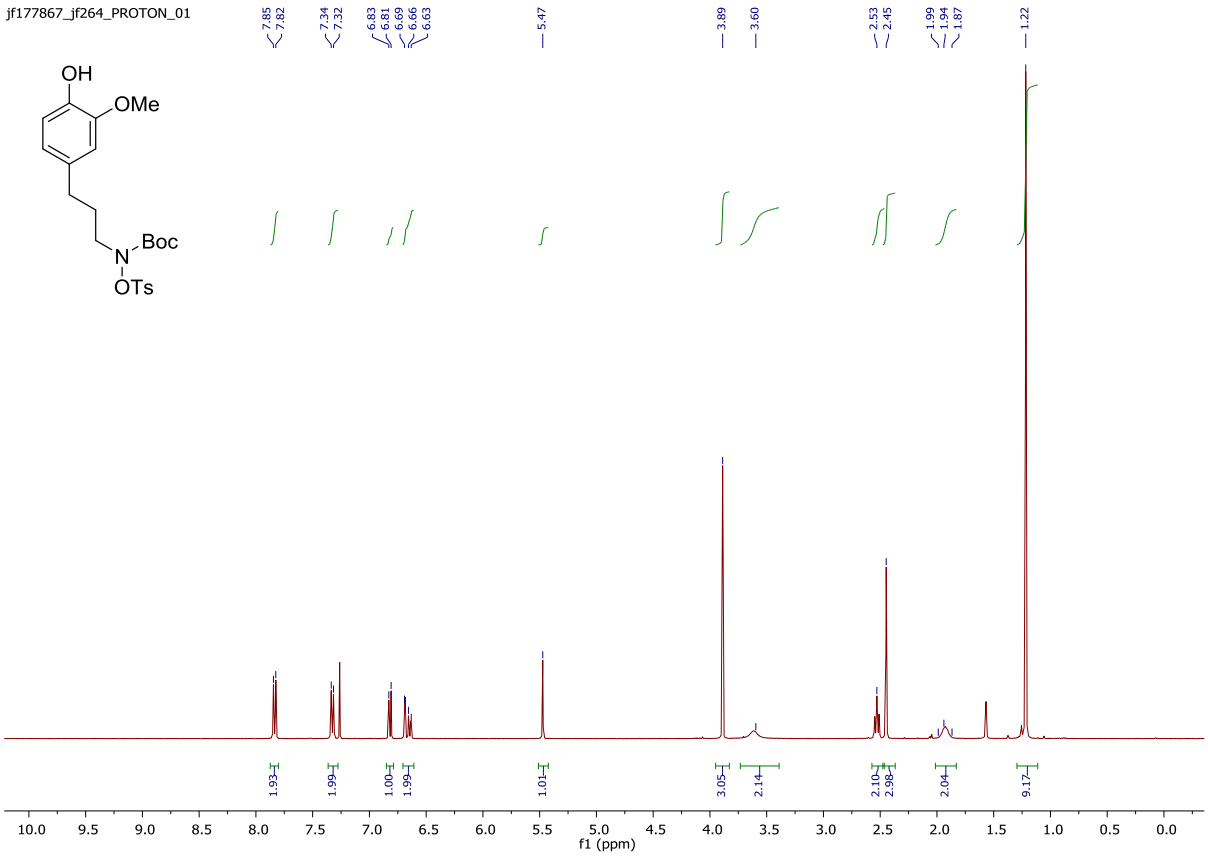


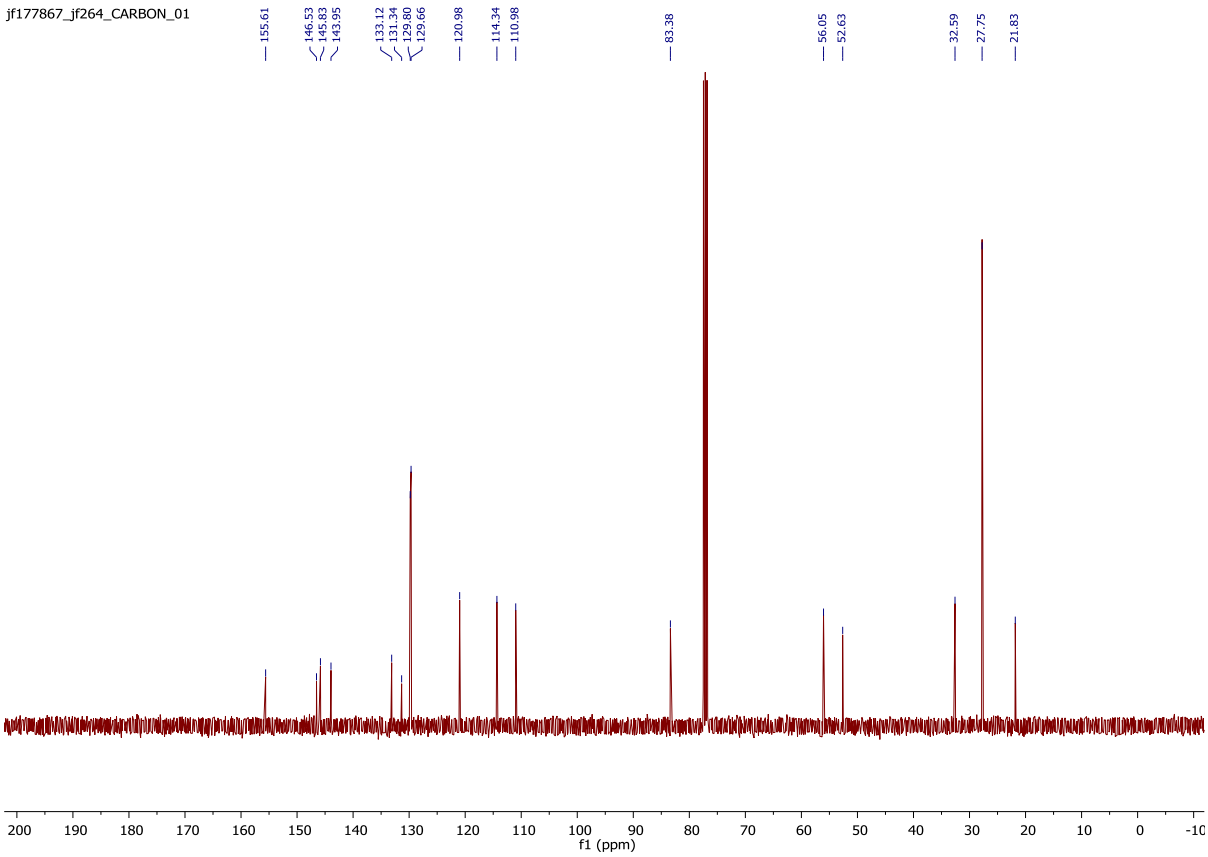
tert-Butyl (3-(4-((_tert_-butyldimethylsilyl)oxy)-3-methoxyphenyl)propyl)(tosyloxy) carbamate



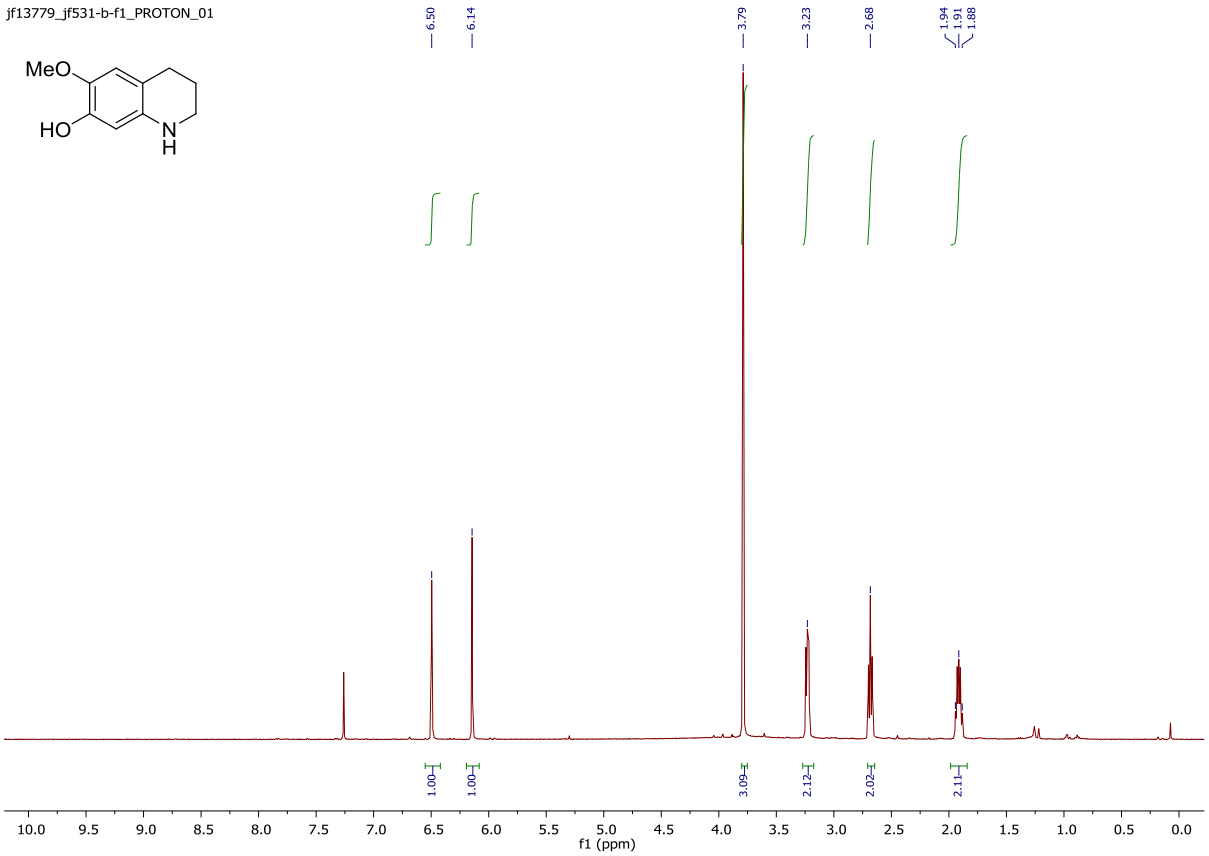


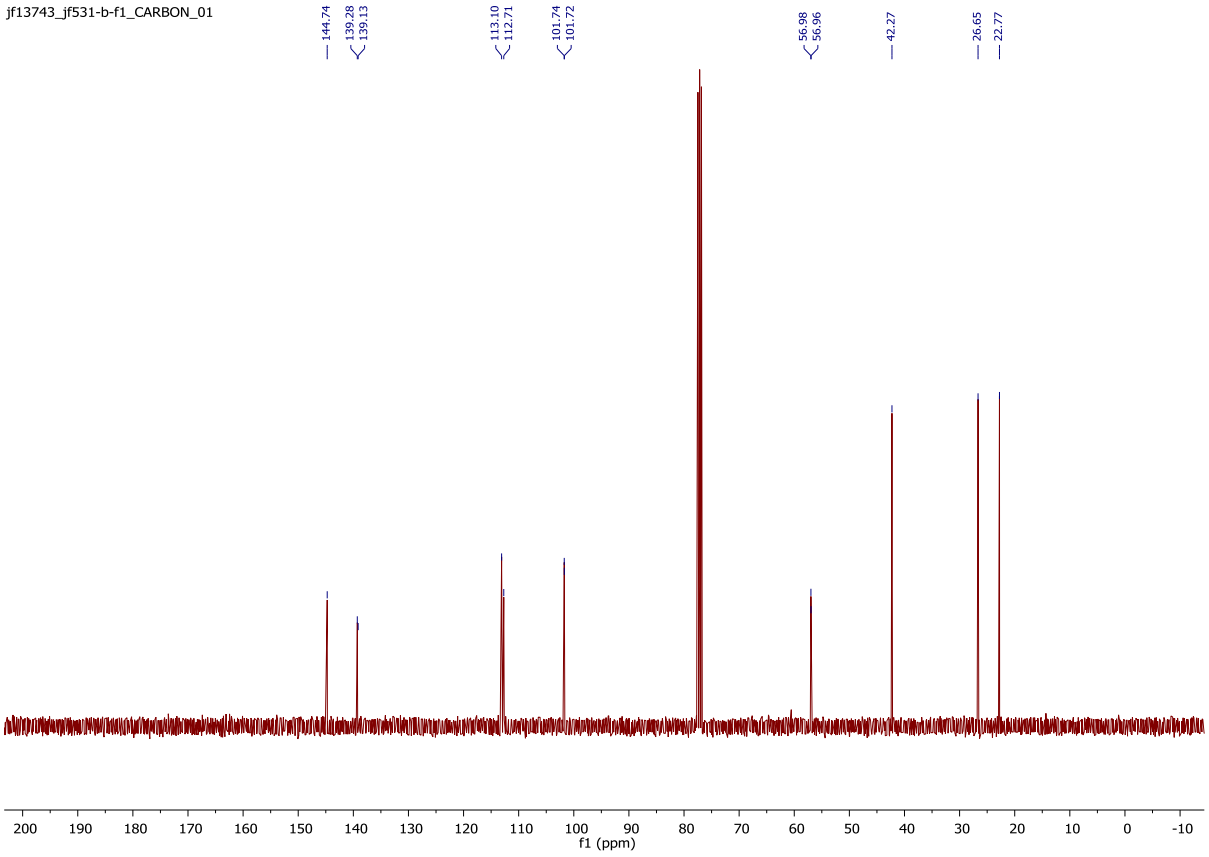
tert-Butyl (3-(4-hydroxy-3-methoxyphenyl)propyl)(tosyloxy)carbamate (5j)



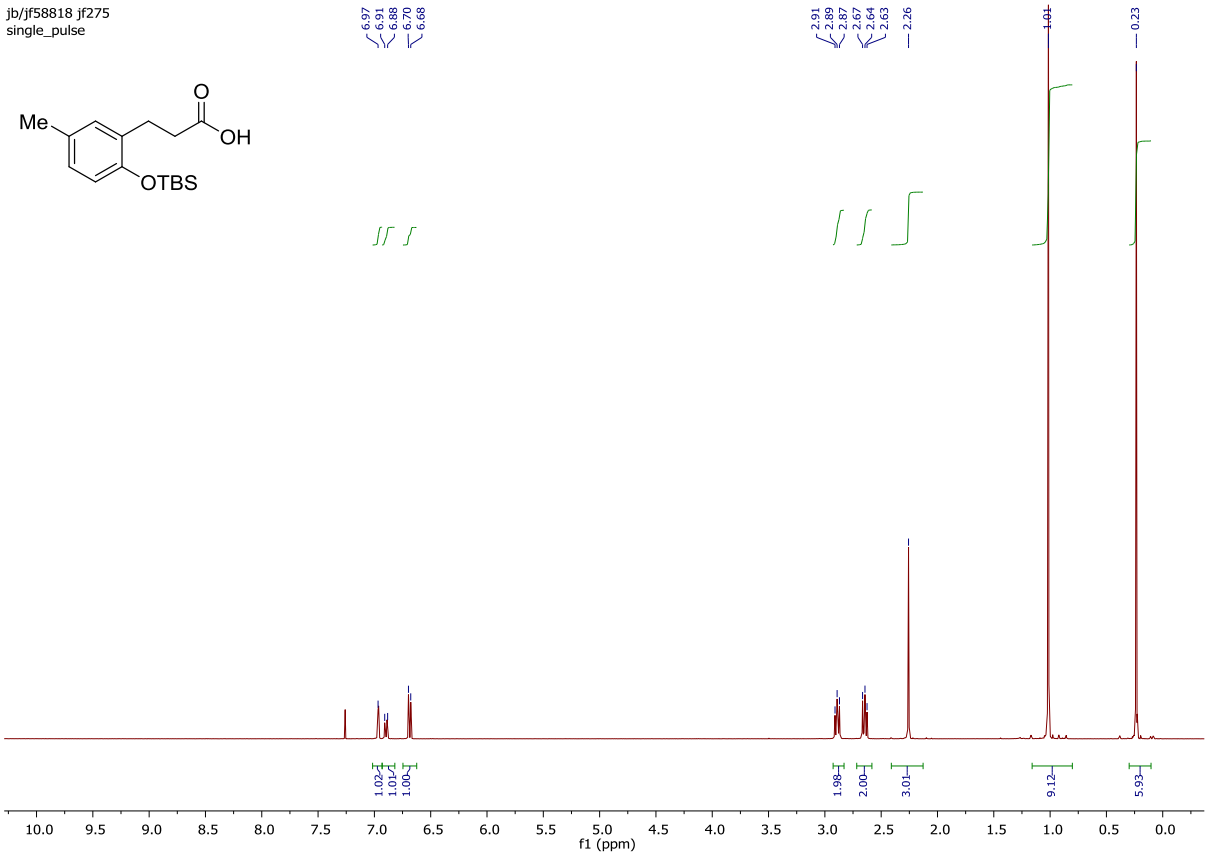


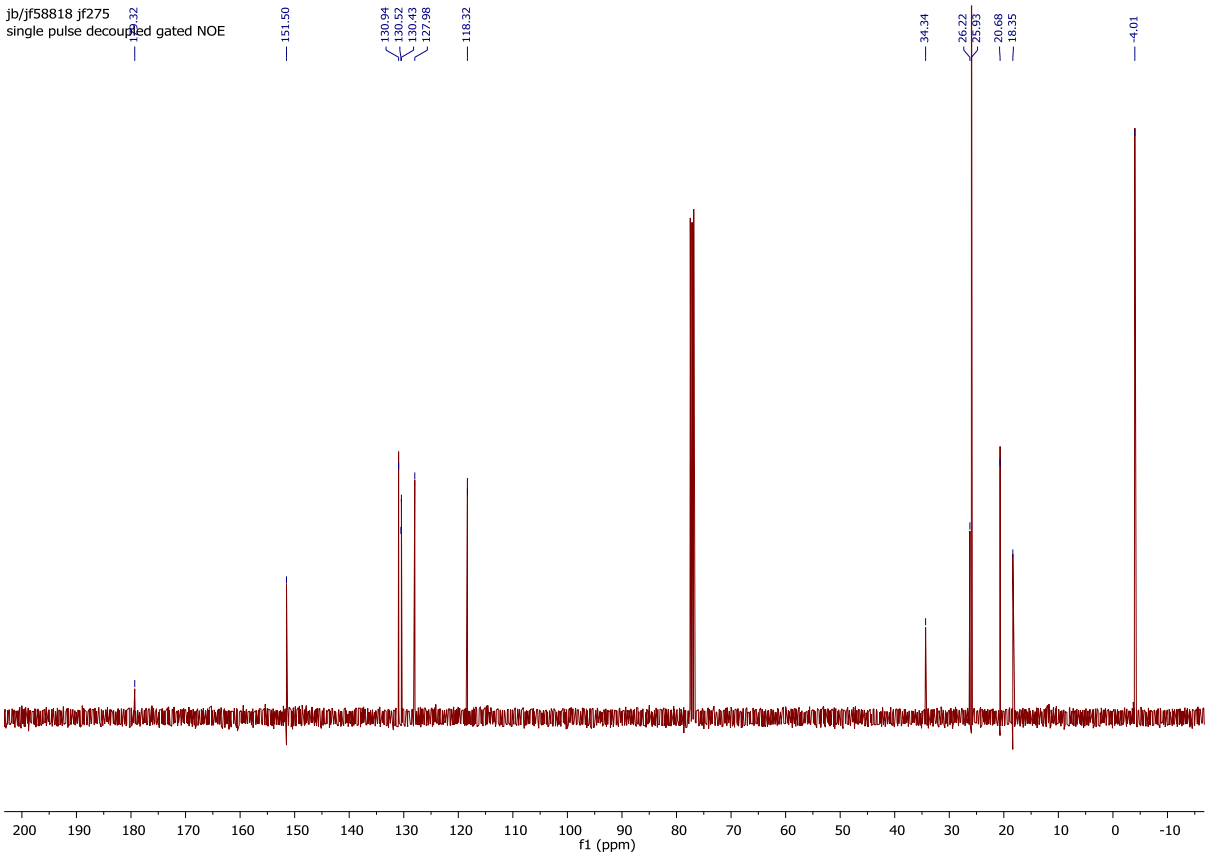
7-methoxy-1,2,3,4-tetrahydroquinolin-6-ol (8j)



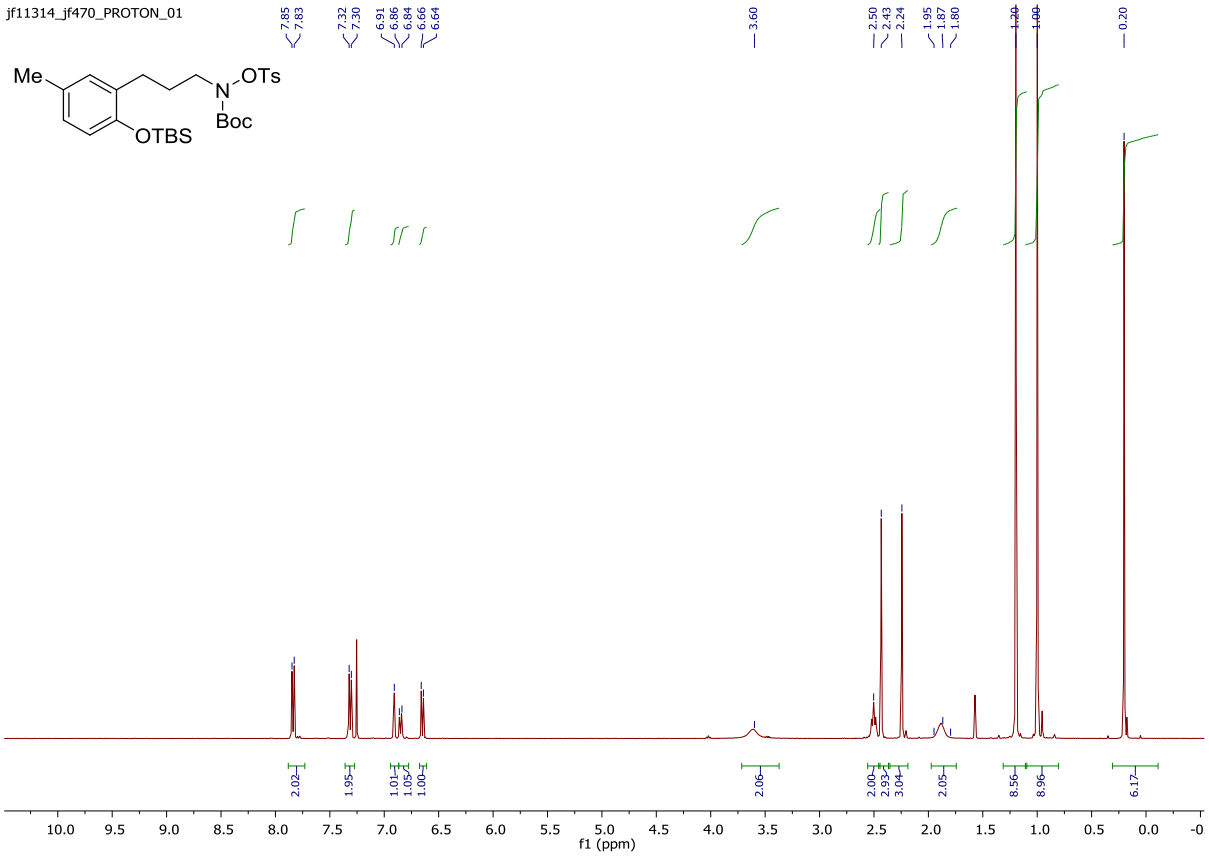


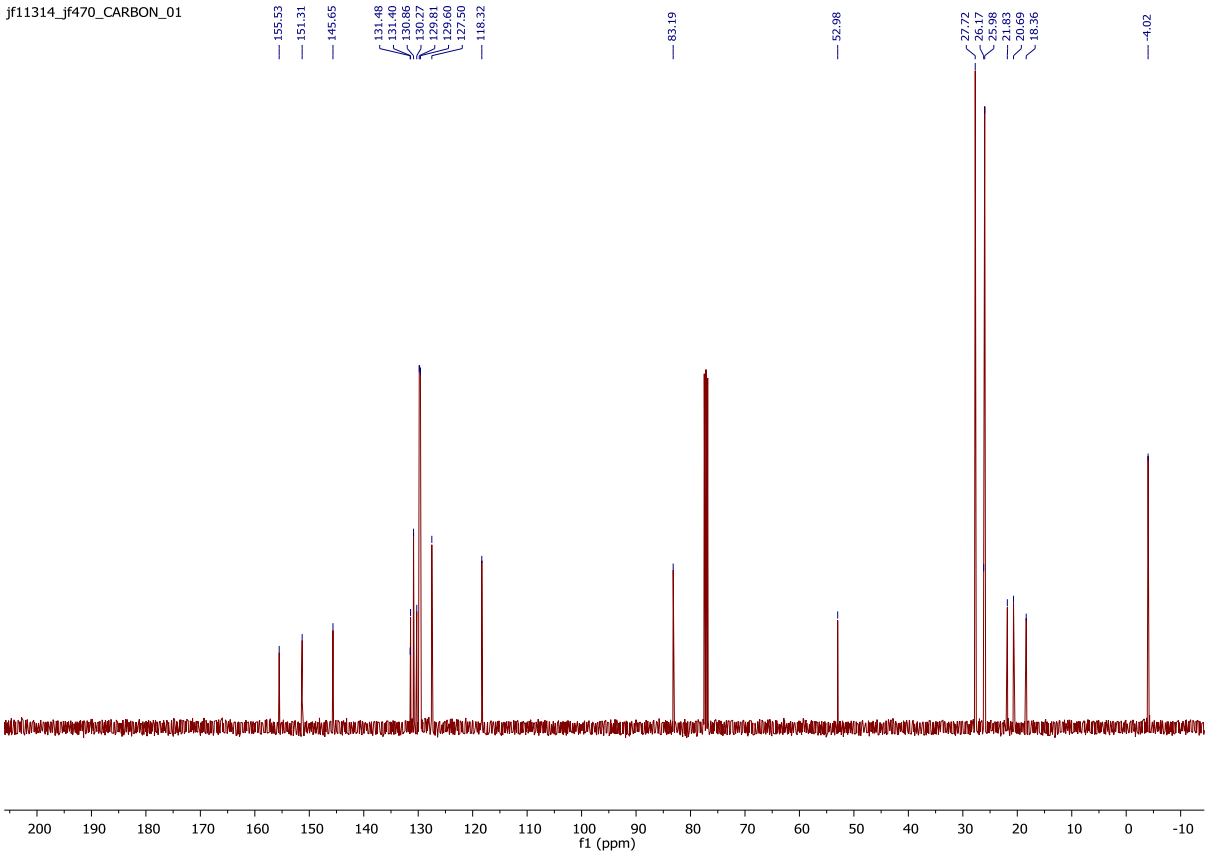
3-(2-((*tert*-Butyldimethylsilyl)oxy)-5-methylphenyl)propanoic acid



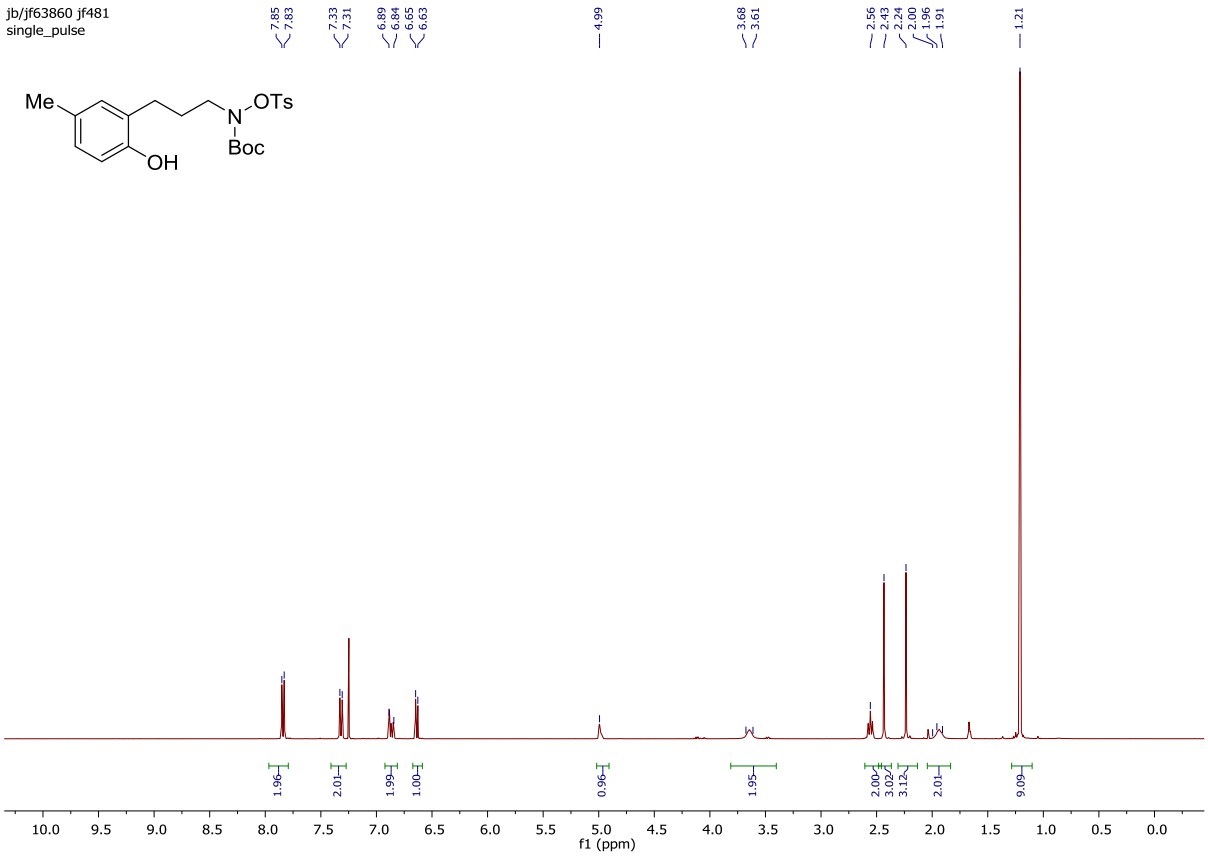


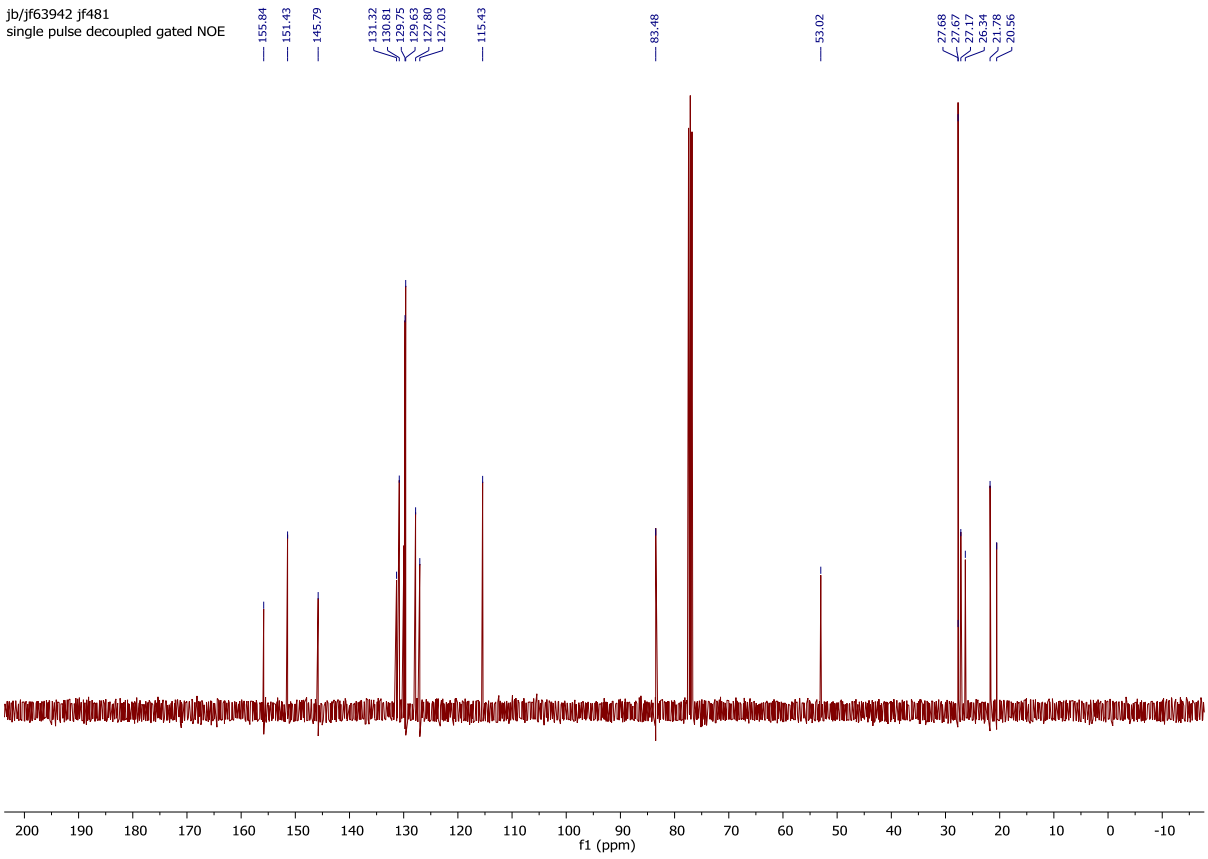
tert-Butyl(3-(2-((_tert_-butyldimethylsilyl)oxy)-5-methylphenyl)propyl)(tosyloxy) carbamate



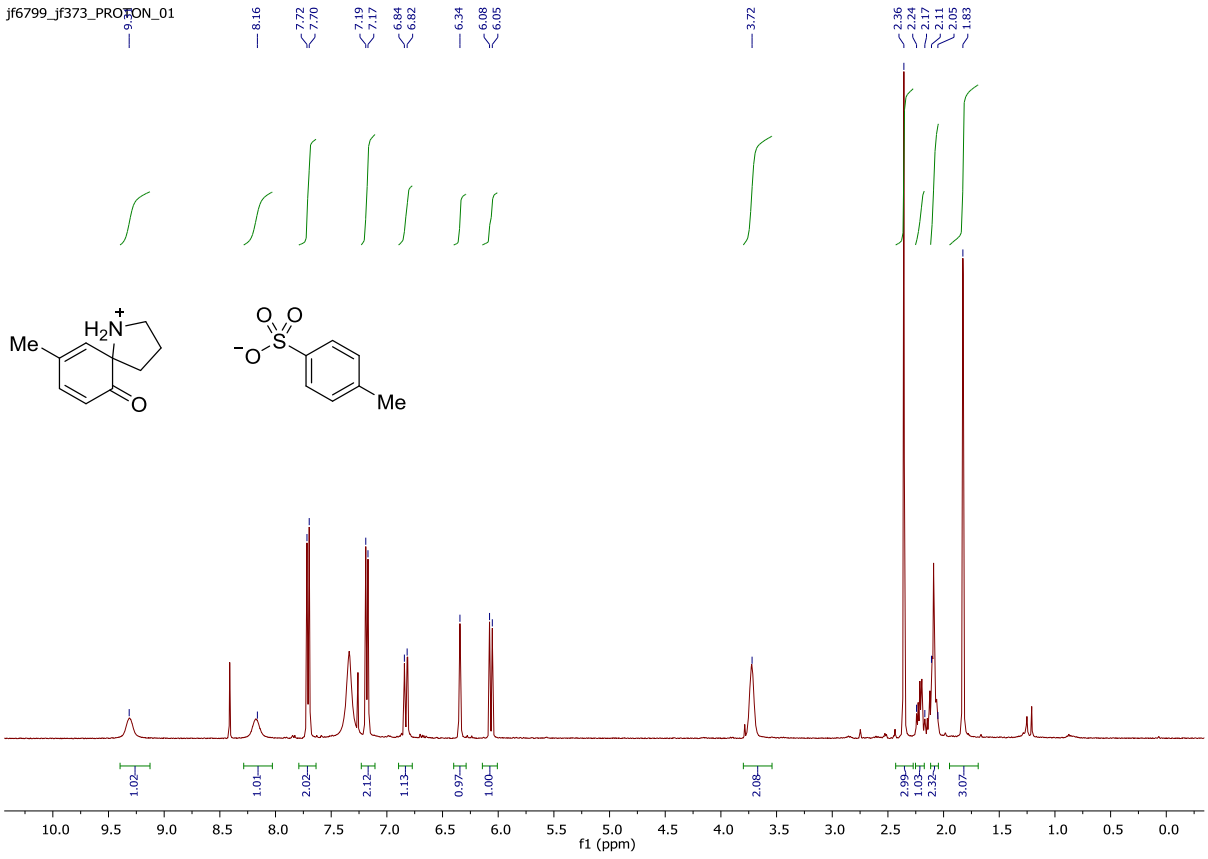


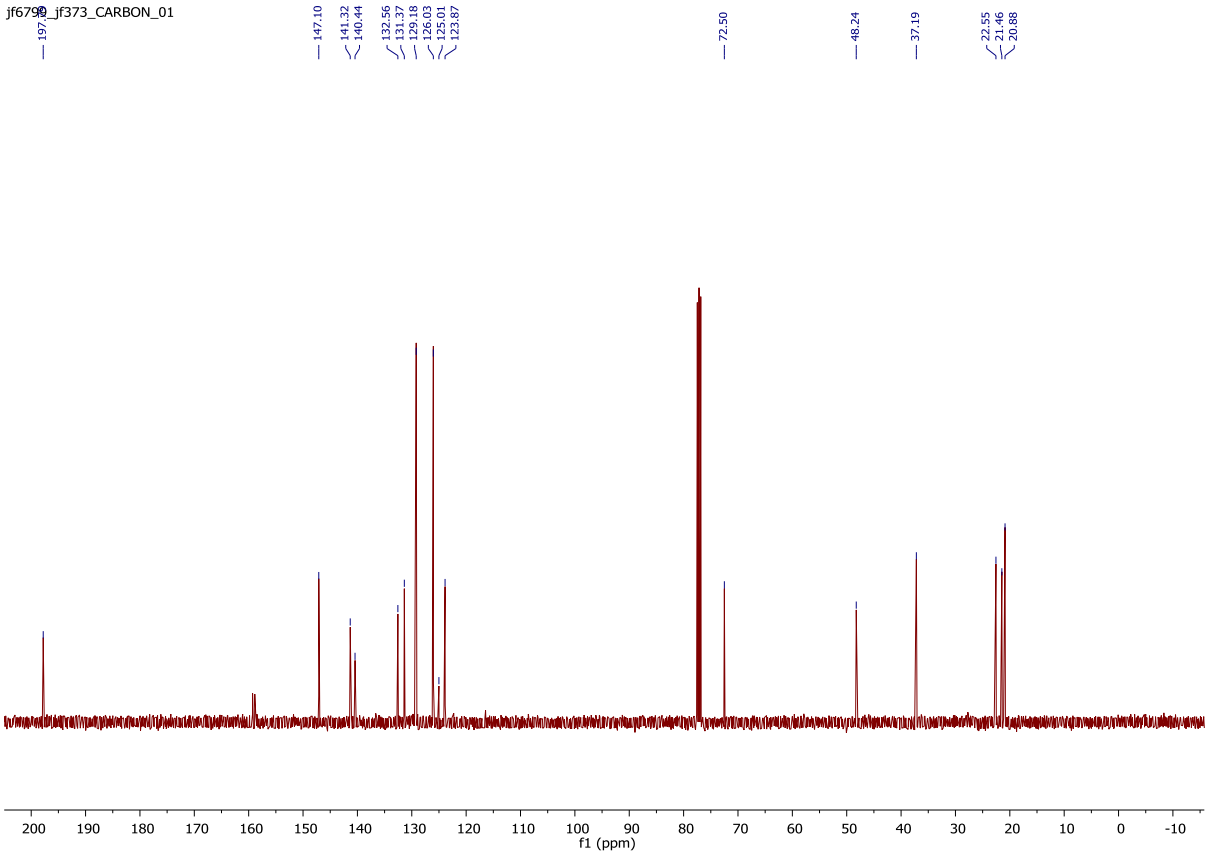
tert-Butyl (3-(2-hydroxy-5-methylphenyl)propyl)(tosyloxy)carbamate (5k)



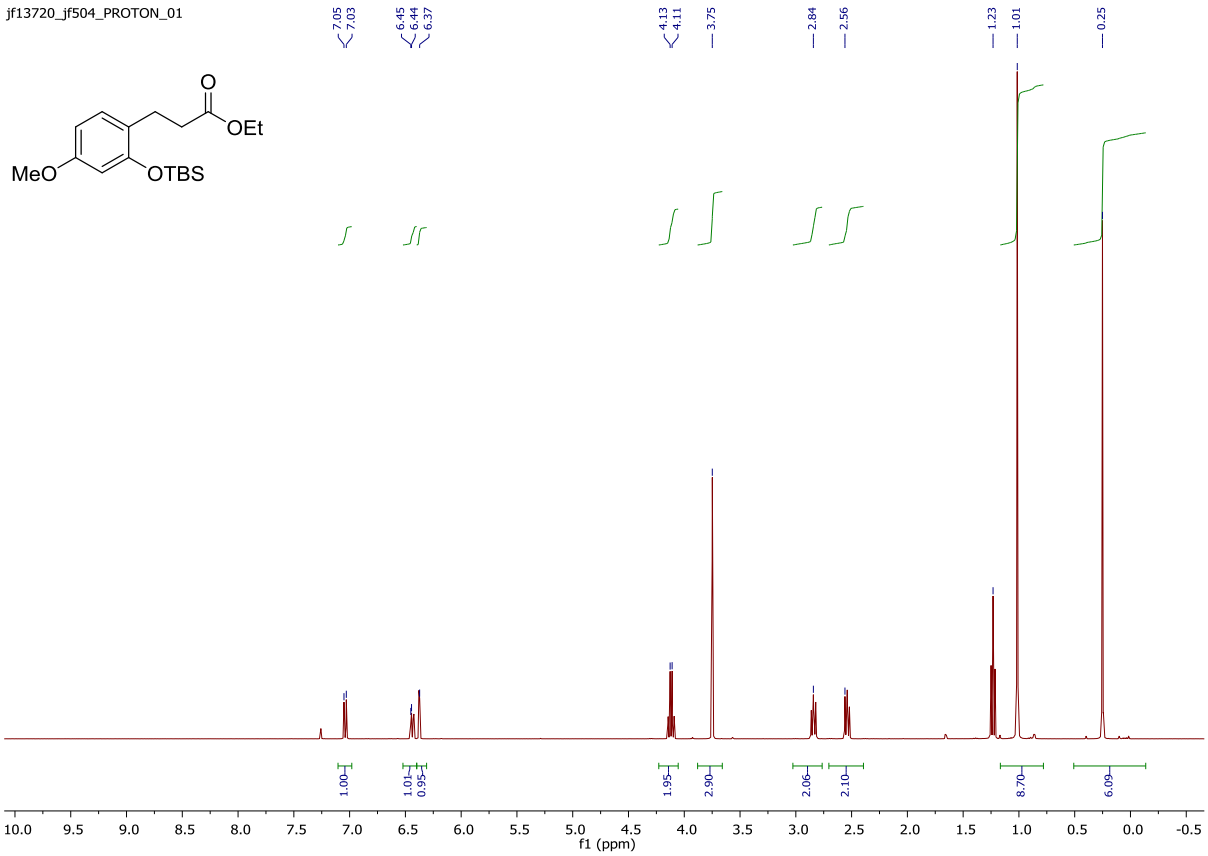


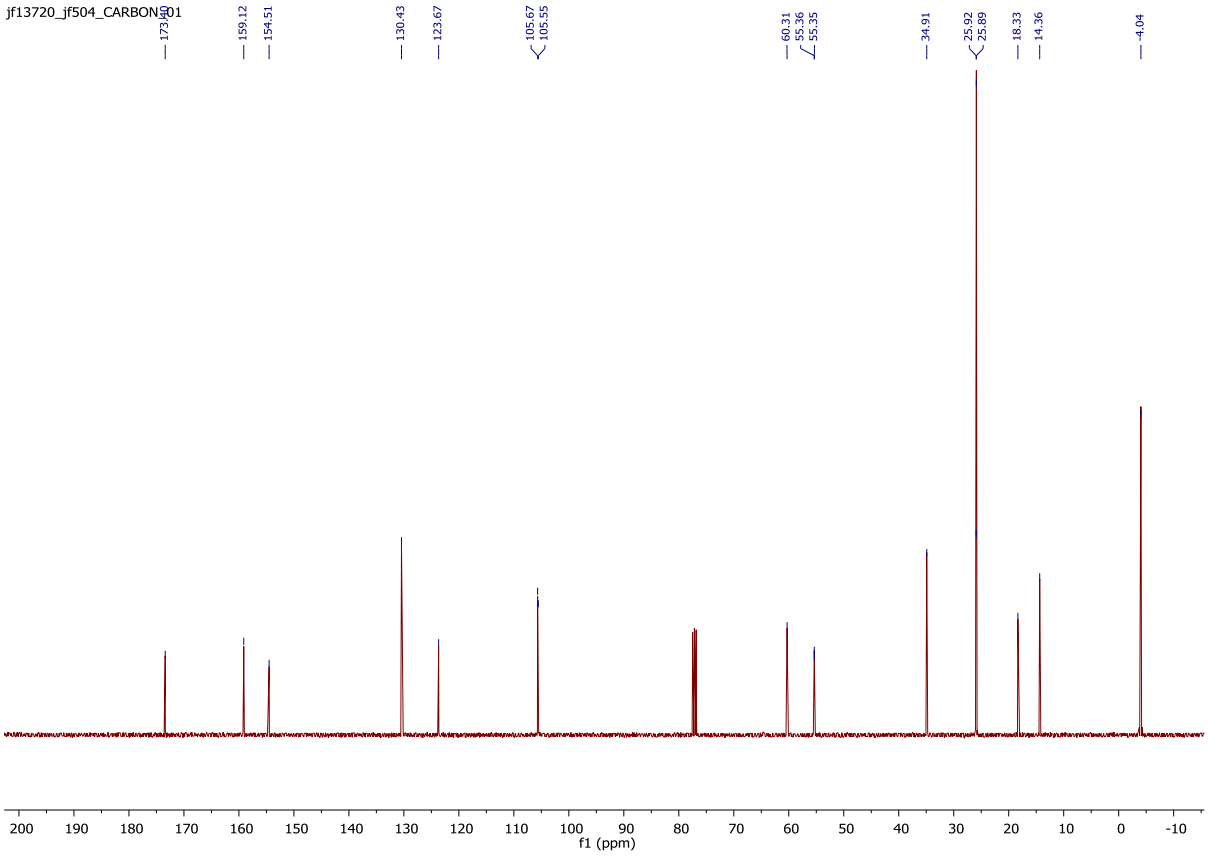
9-Methyl-1-azaspiro[4.5]deca-7,9-dien-6-one tosylate (7k)



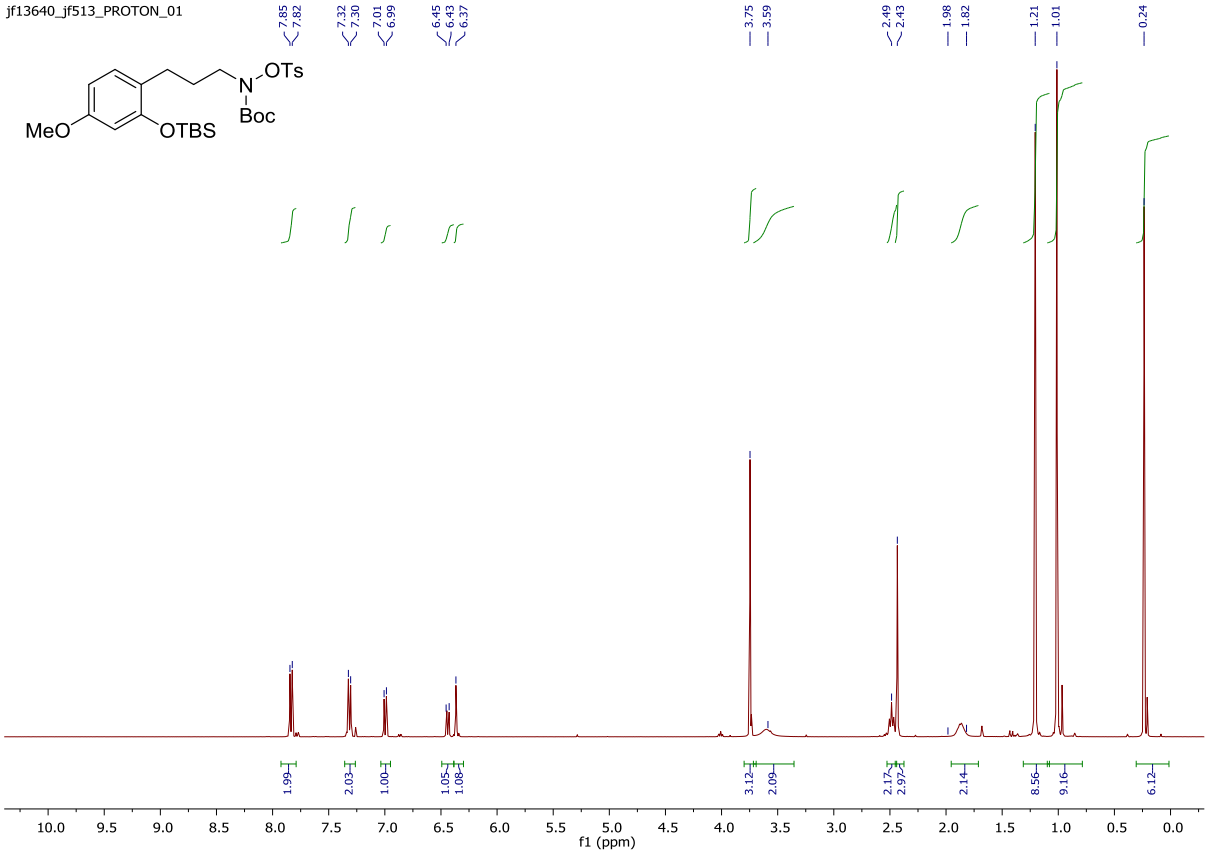


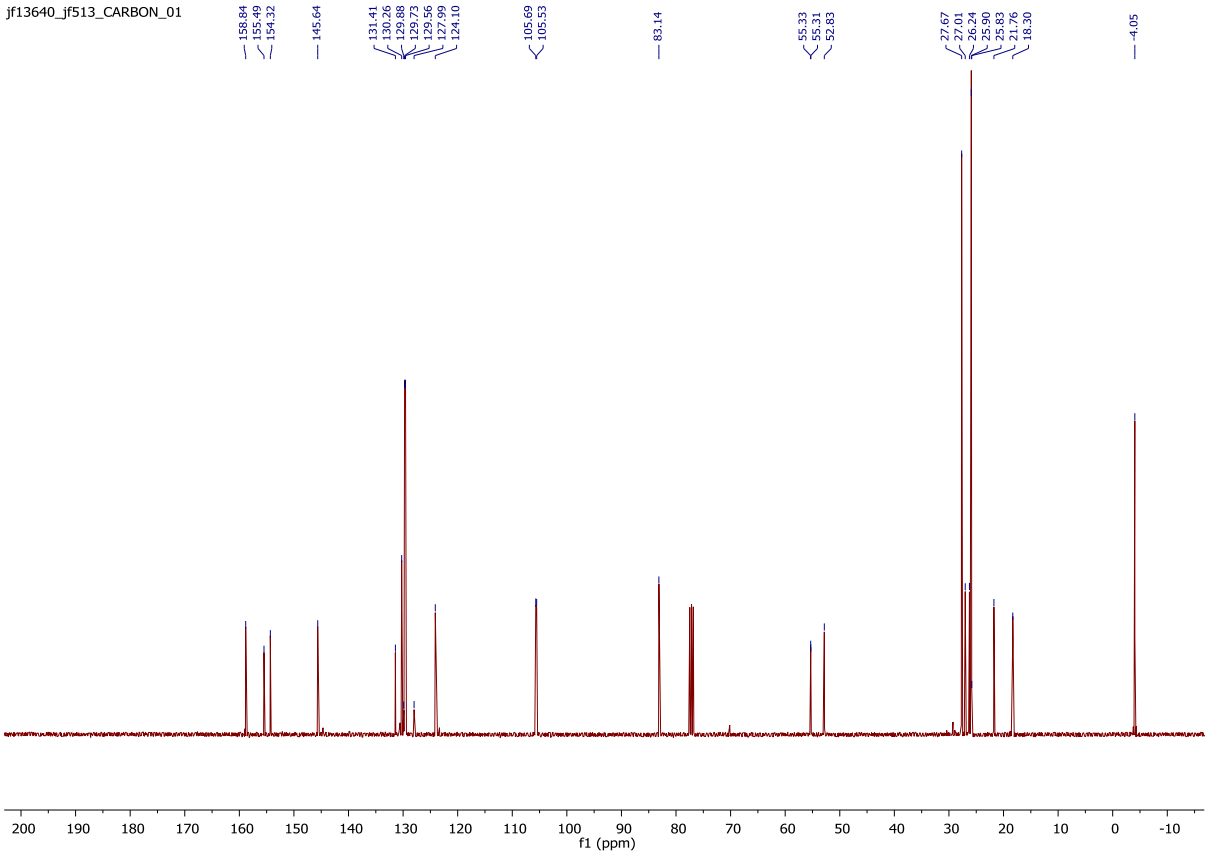
Ethyl 3-(2-((*tert*-butyldimethylsilyl)oxy)-4-methoxyphenyl)propanoate



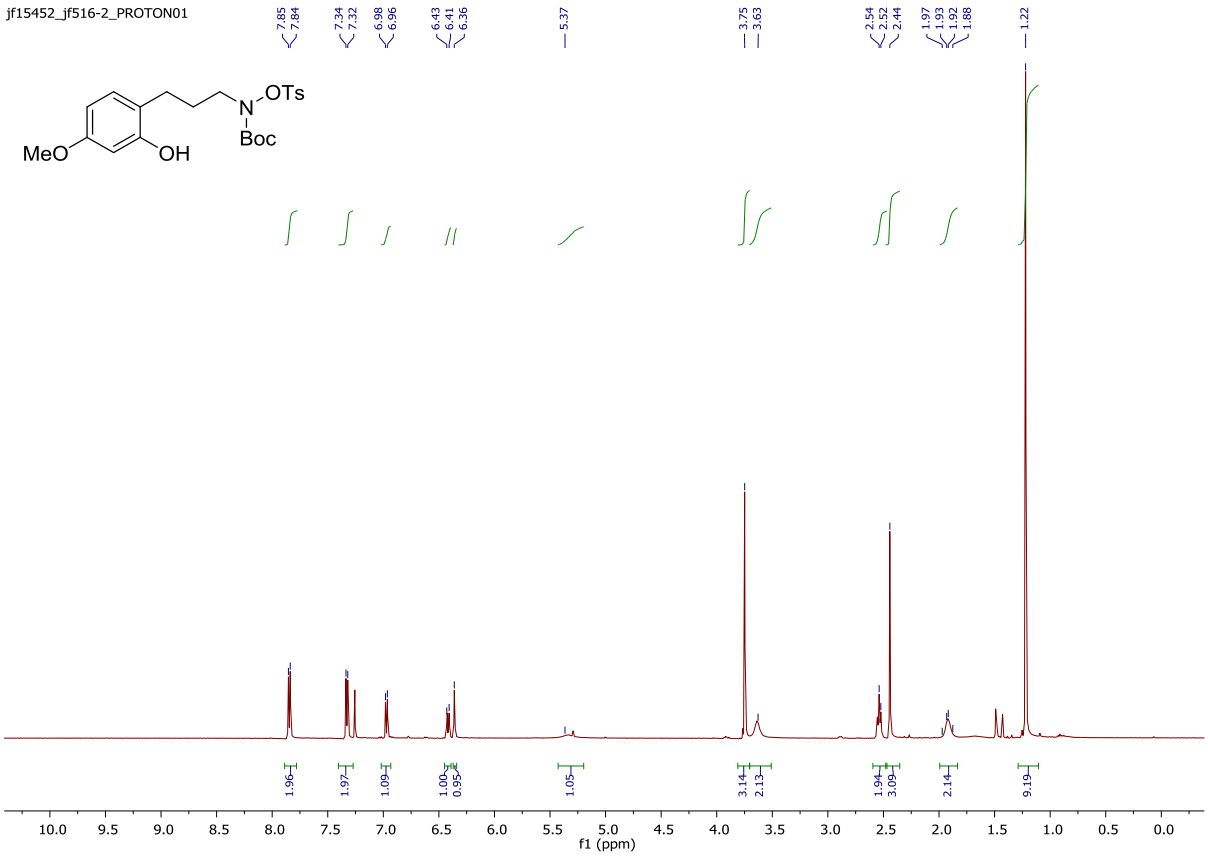


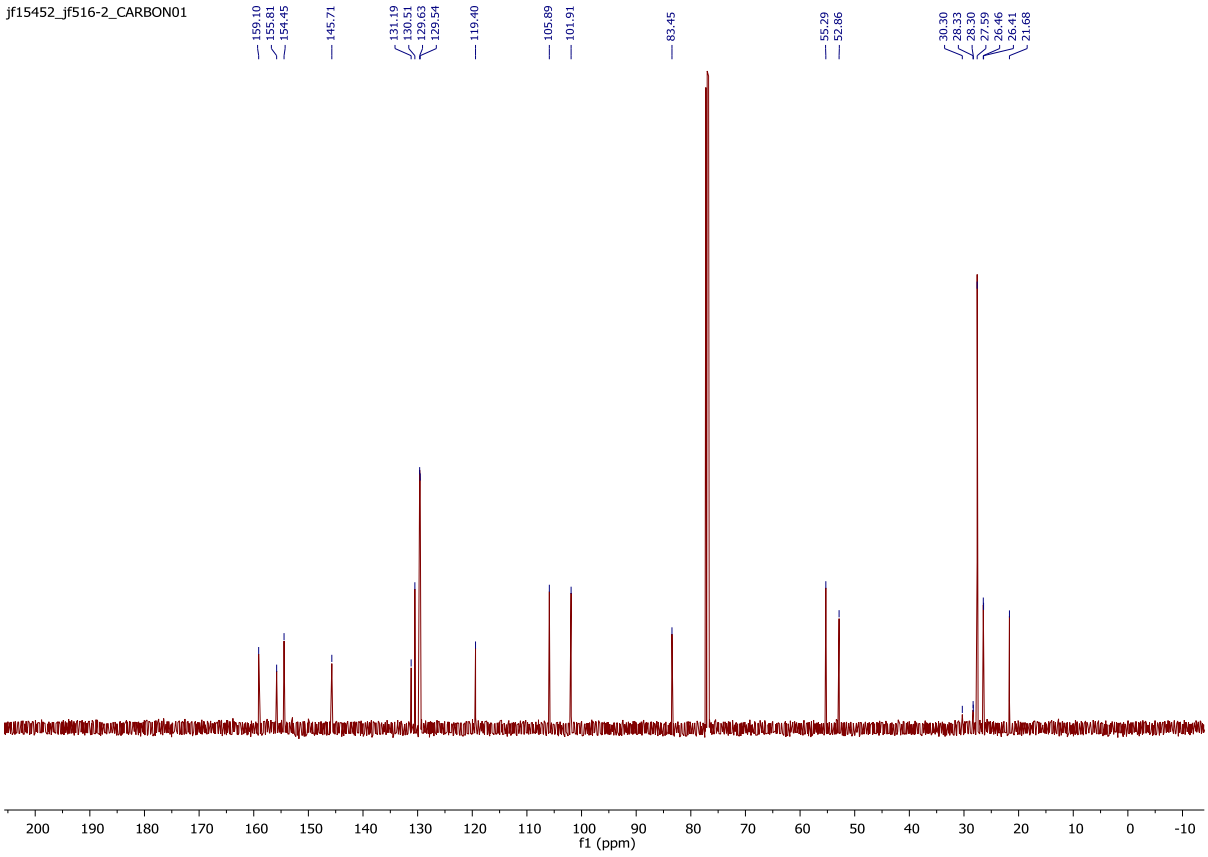
tert-Butyl (3-(2-((_tert_-butyldimethylsilyl)oxy)-4-methoxyphenyl)propyl)(tosyloxy) carbamate



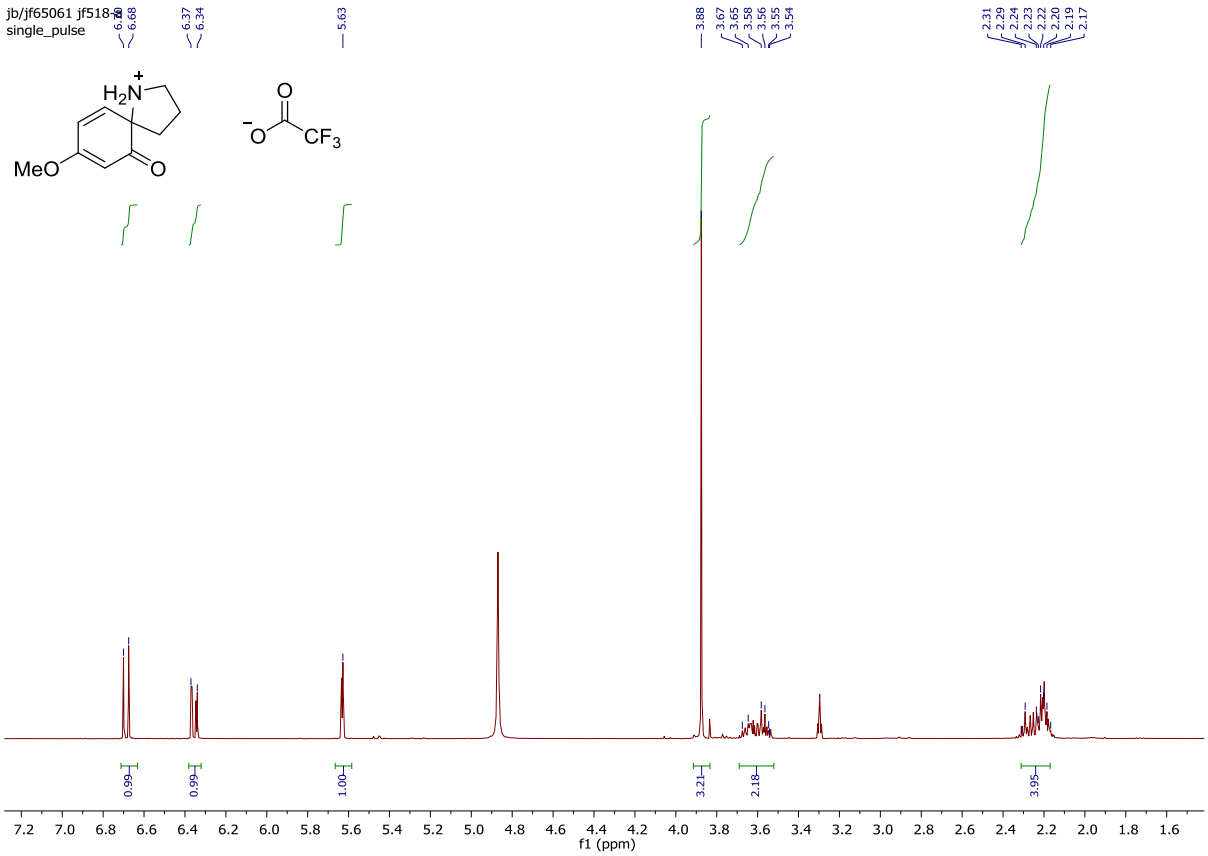


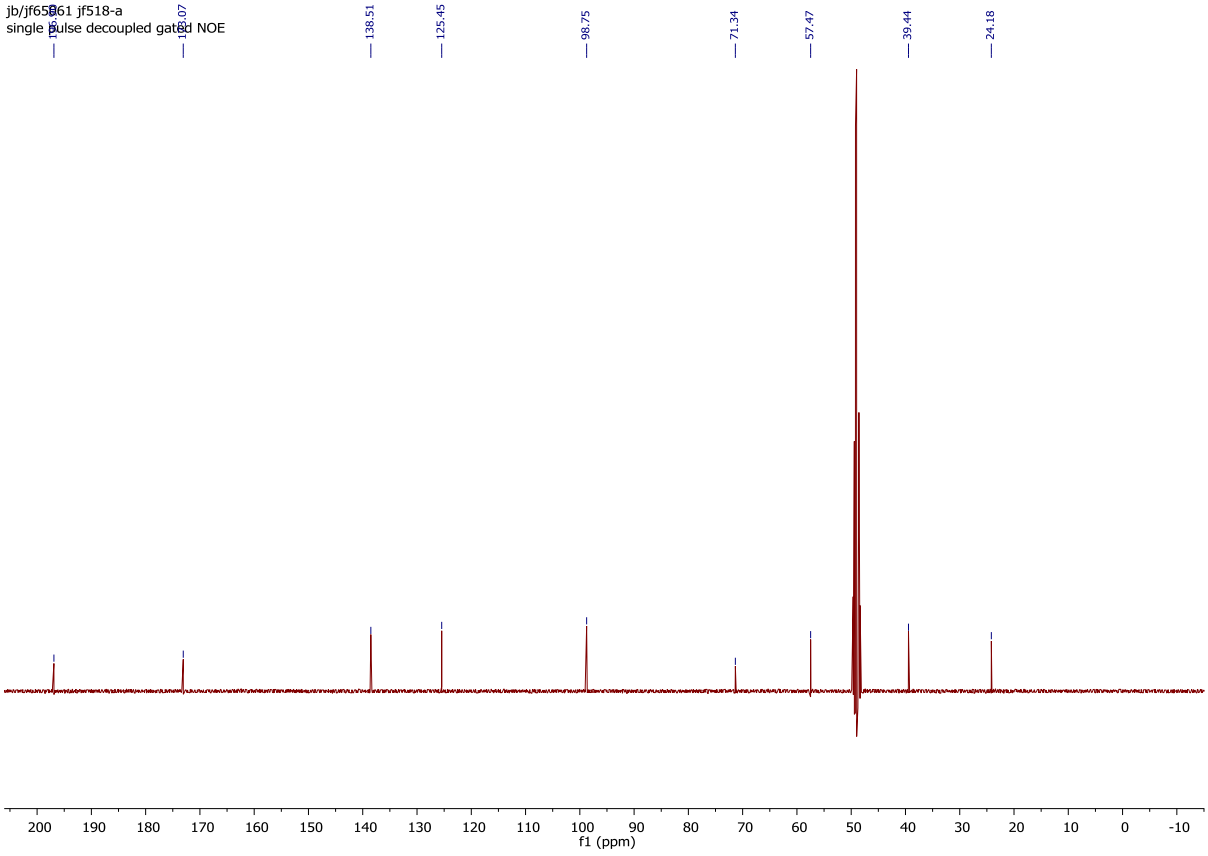
tert-Butyl (3-(2-hydroxy-4-methoxyphenyl)propyl)(tosyloxy)carbamate (5l)



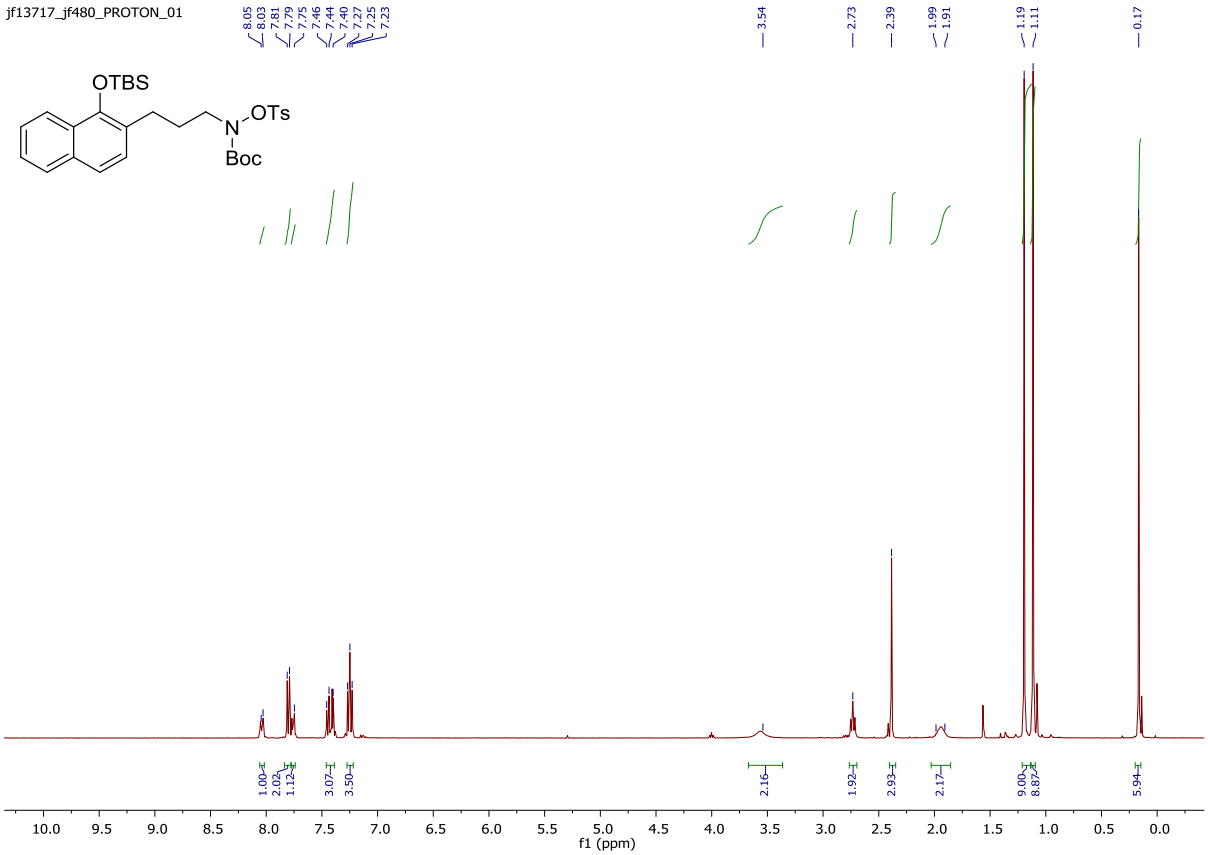


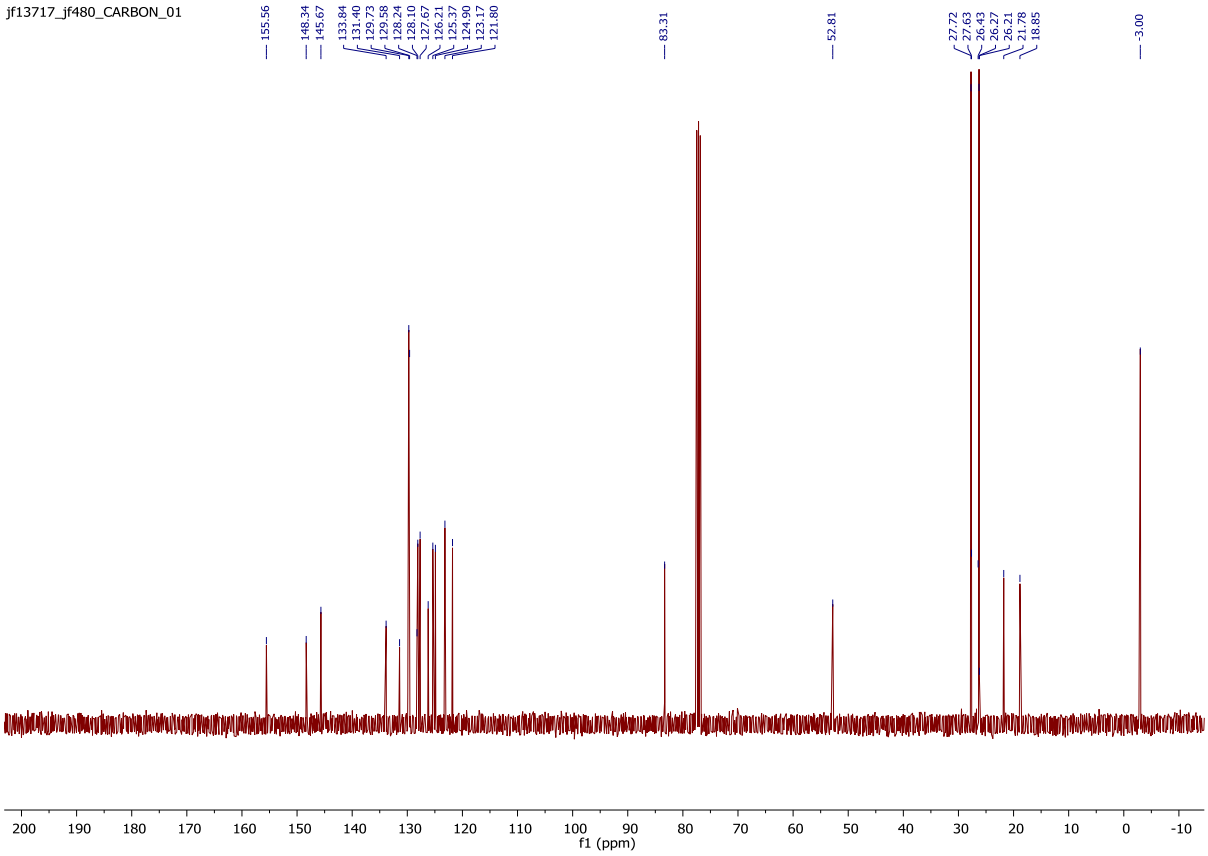
8-Methoxy-1-azaspiro[4.5]deca-7,9-dien-6-one trifluoroacetate (7l)



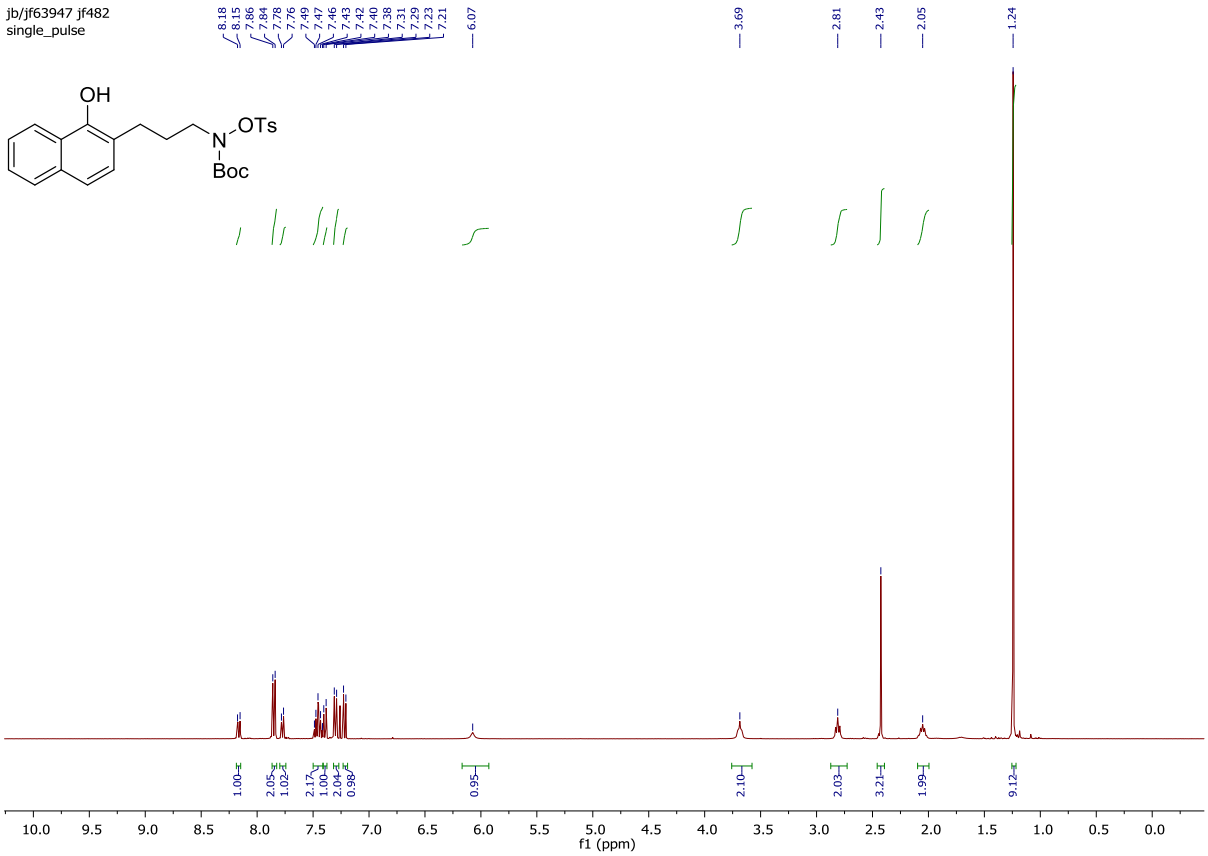


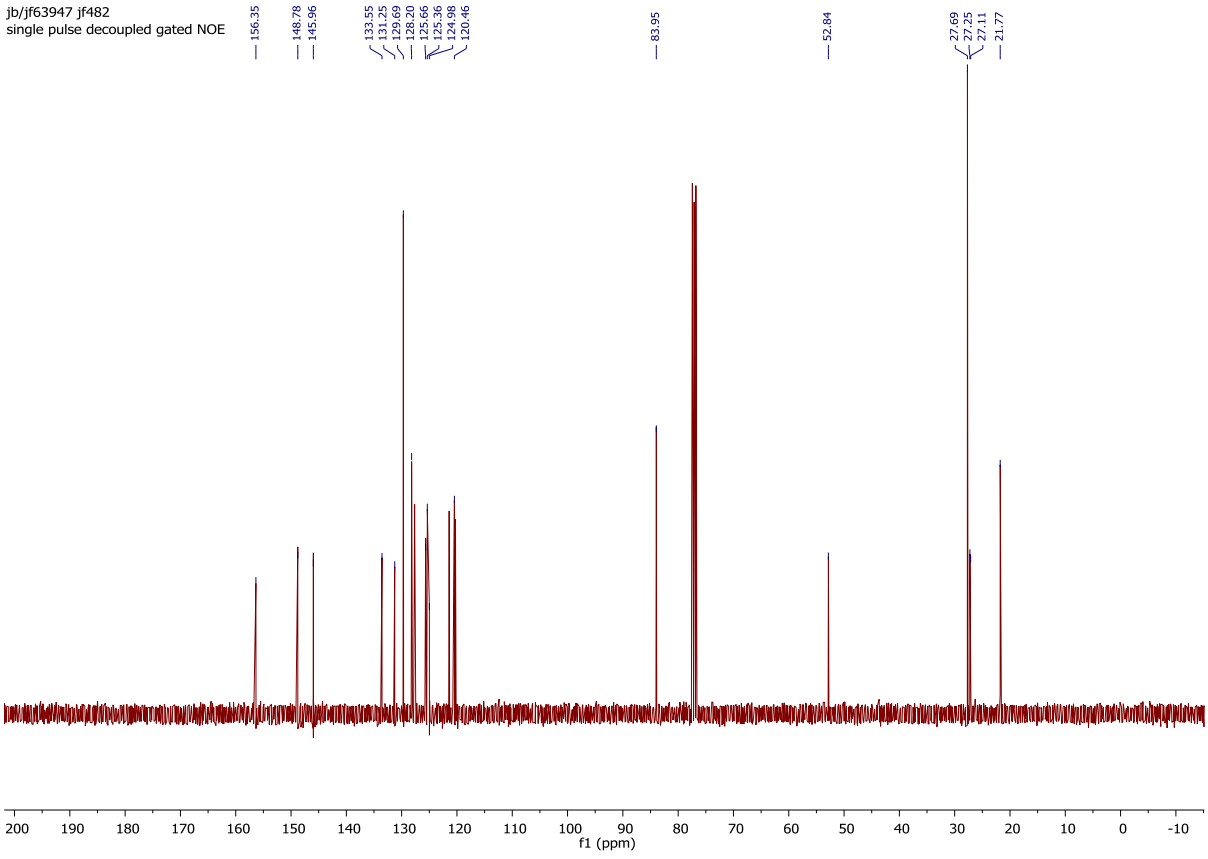
tert-Butyl (3-(1-((_tert_-butyldimethylsilyl)oxy)naphthalen-2-yl)propyl)(tosyloxy) carbamate



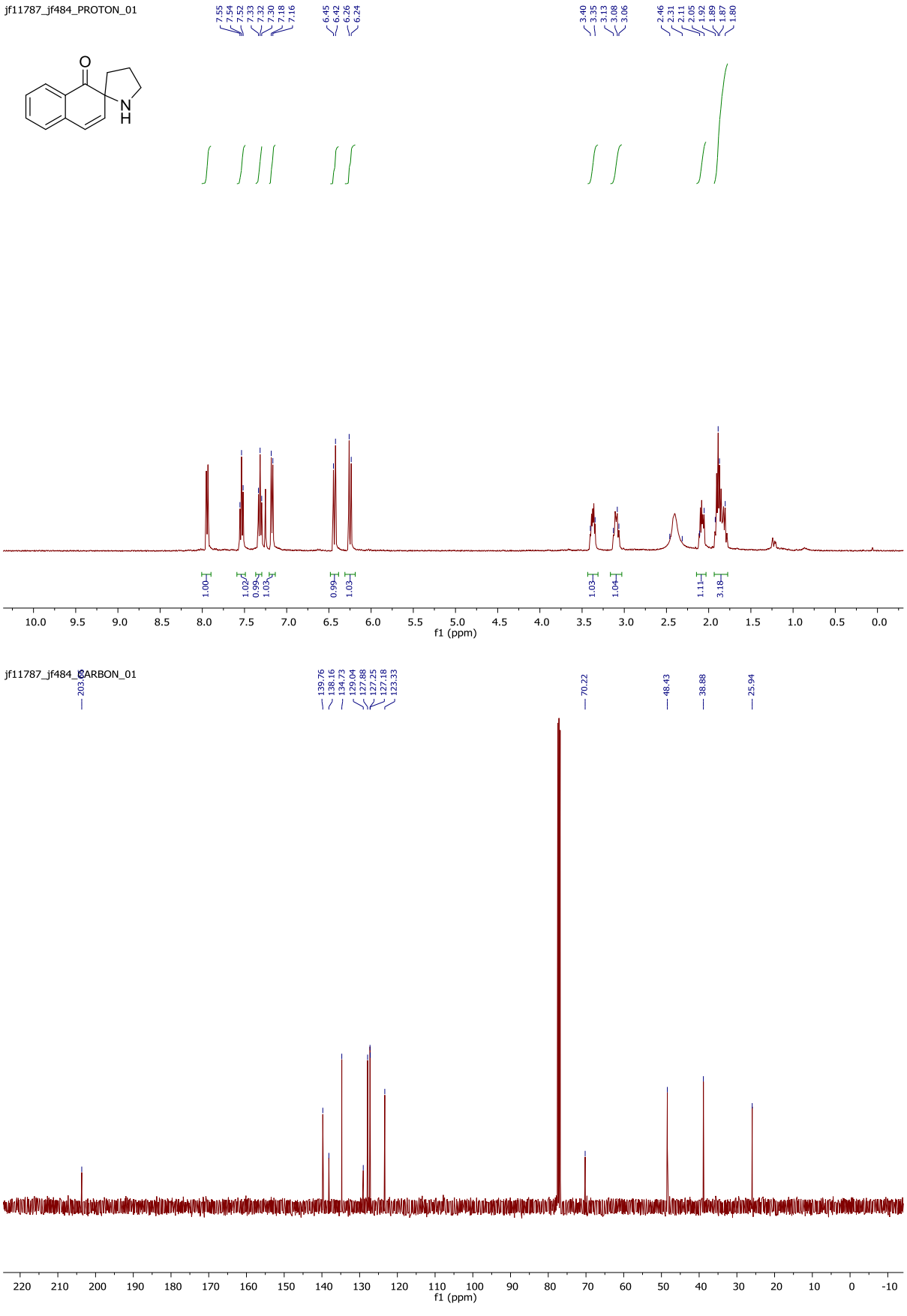


tert-Butyl (3-(1-hydroxynaphthalen-2-yl)propyl)(tosyloxy)carbamate (5m)

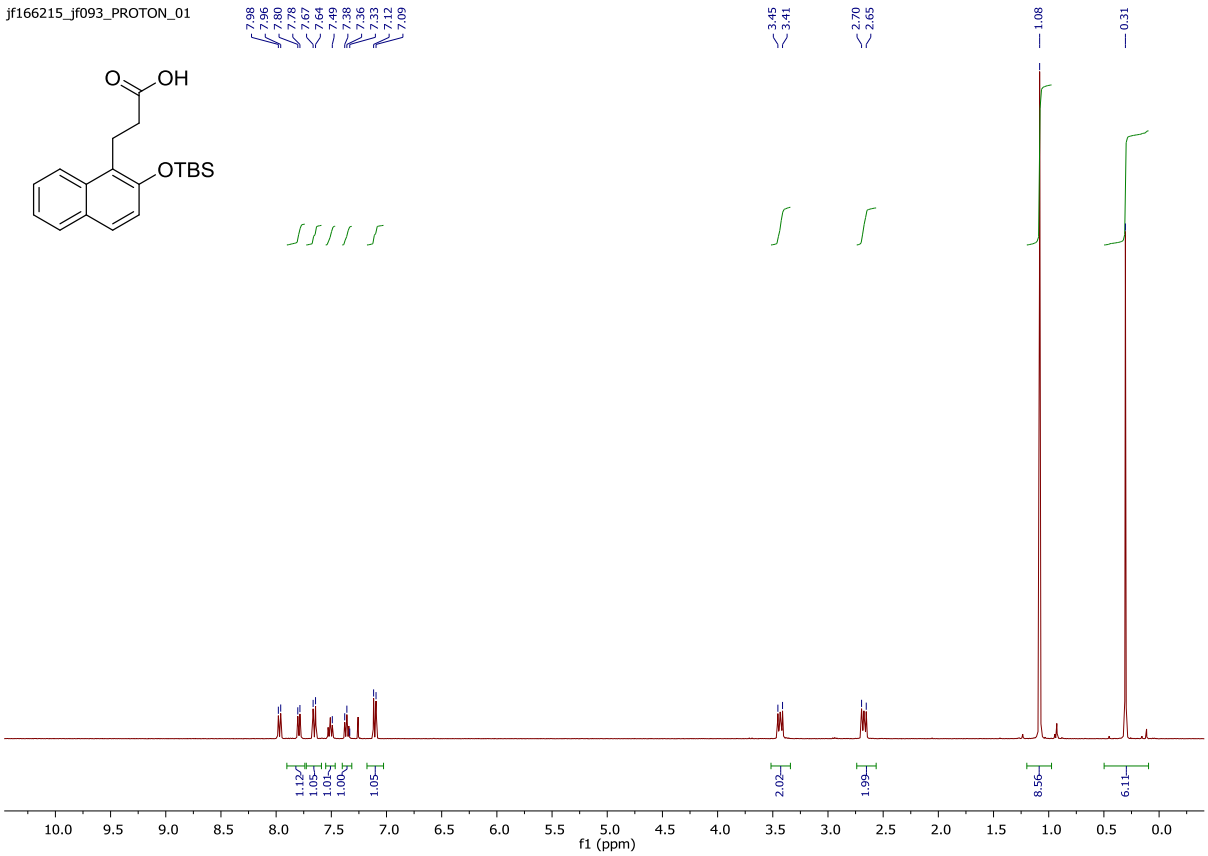


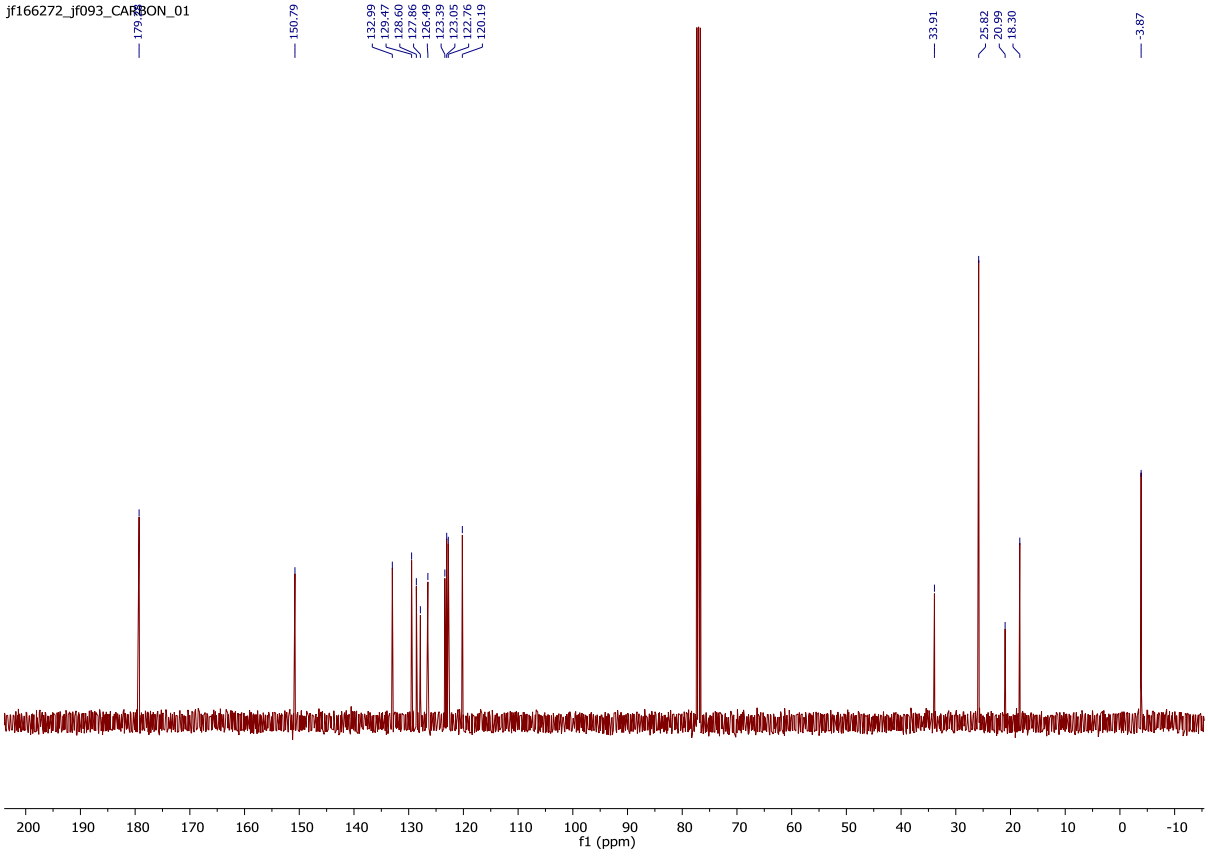


1H-spiro[naphthalene-2,2'-pyrrolidin]-1-one (7m)

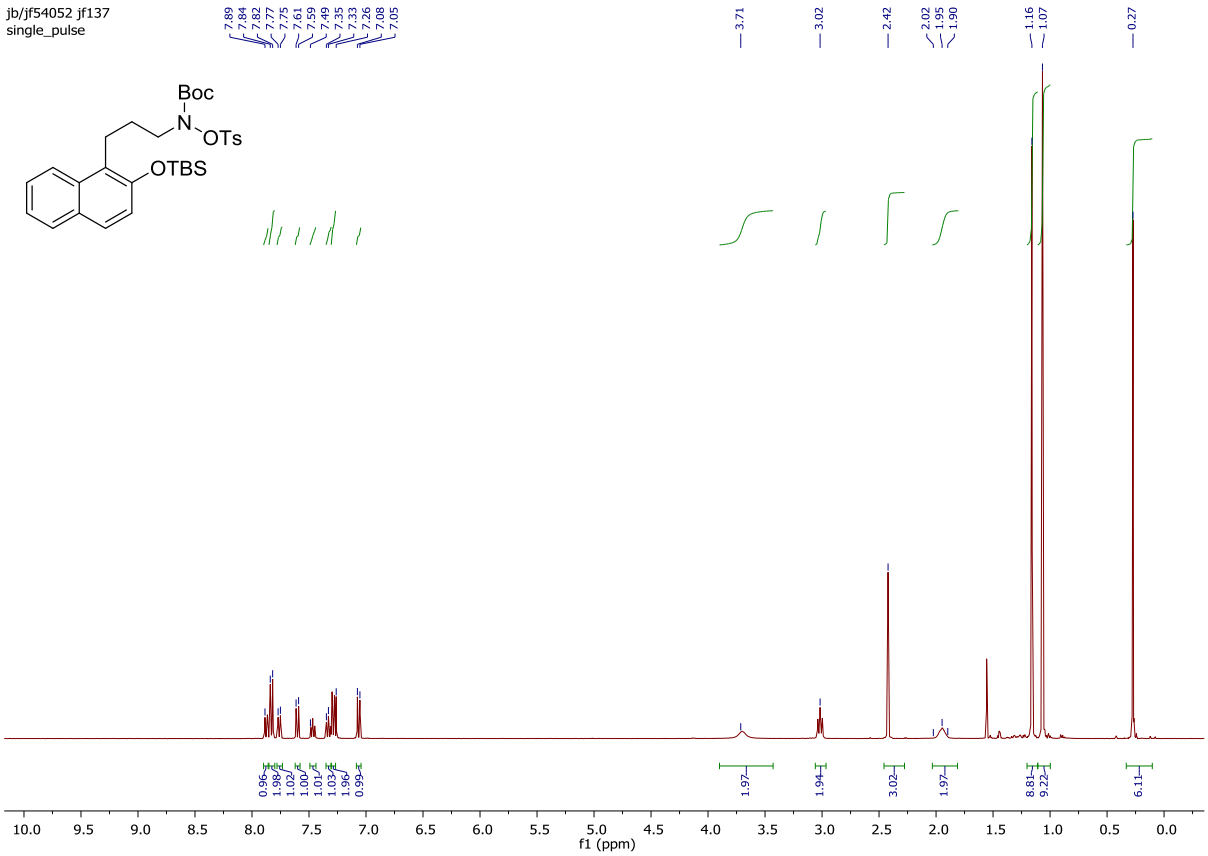


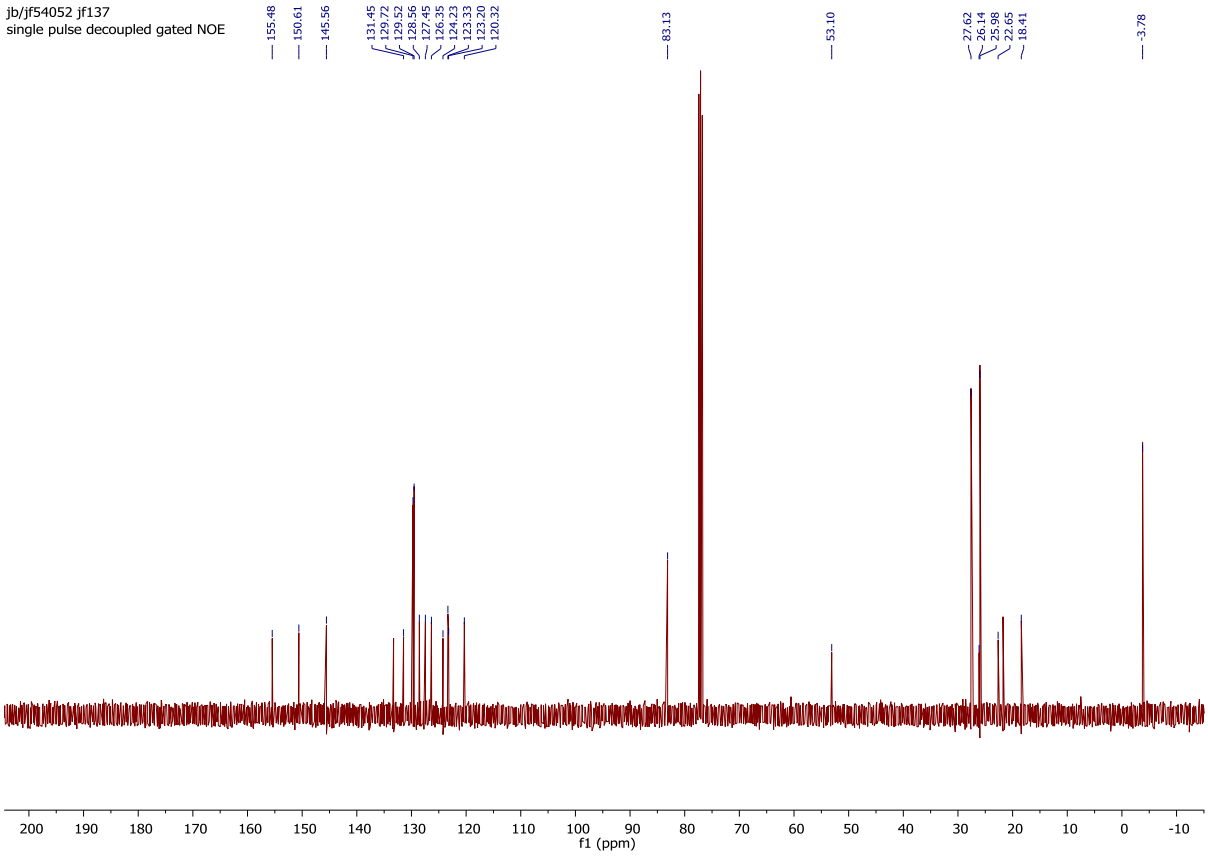
3-(2-((*tert*-Butyldimethylsilyl)oxy)naphthalen-1-yl)propanoic acid



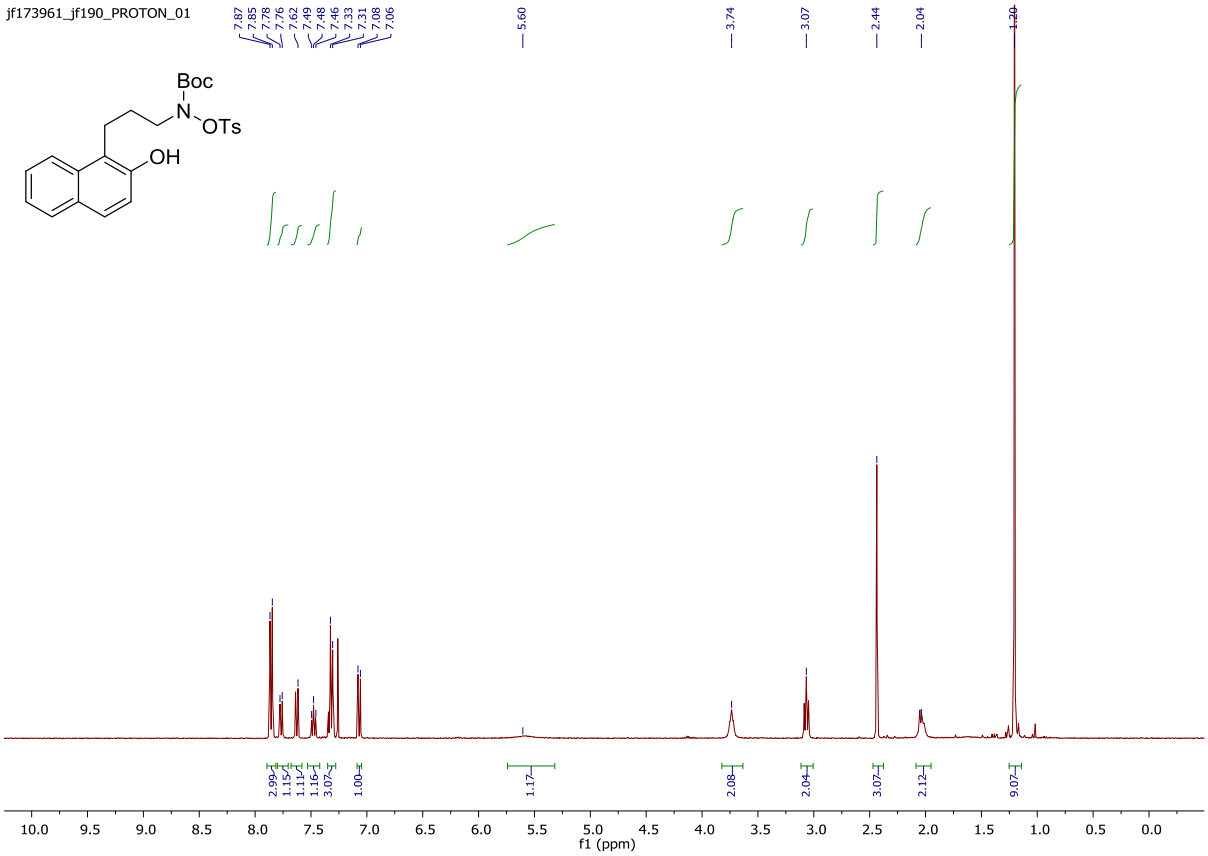


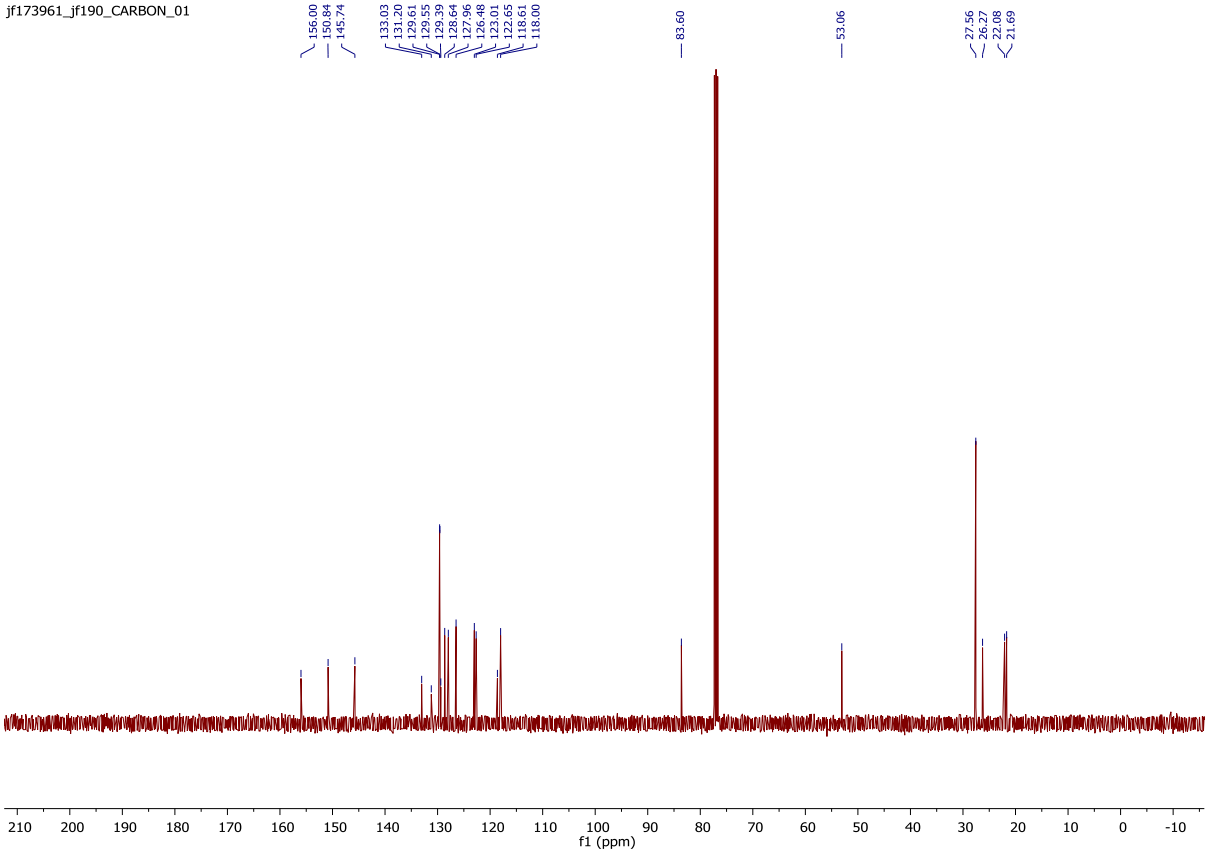
tert-Butyl(3-(2-((*tert*-butyldimethylsilyl)oxy)naphthalen-1-yl)propyl)(tosyloxy) carbamate



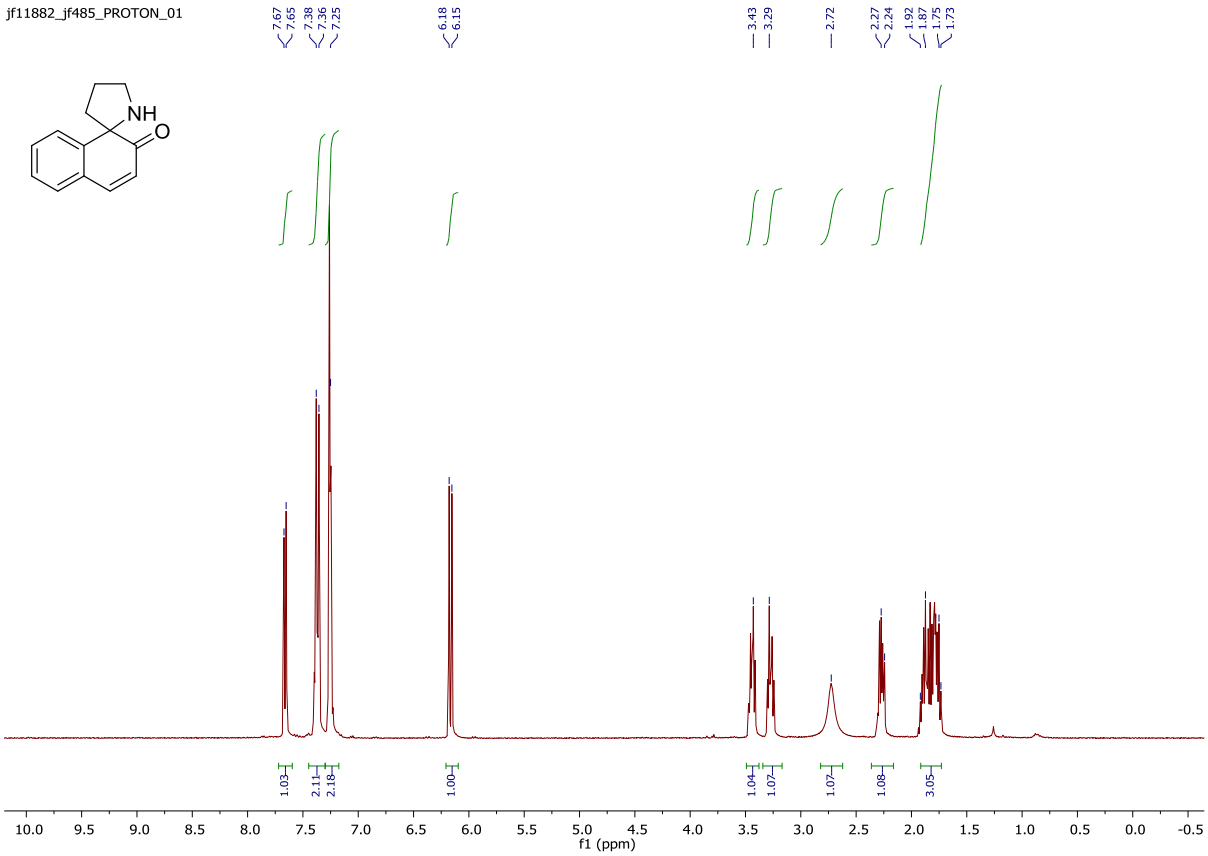


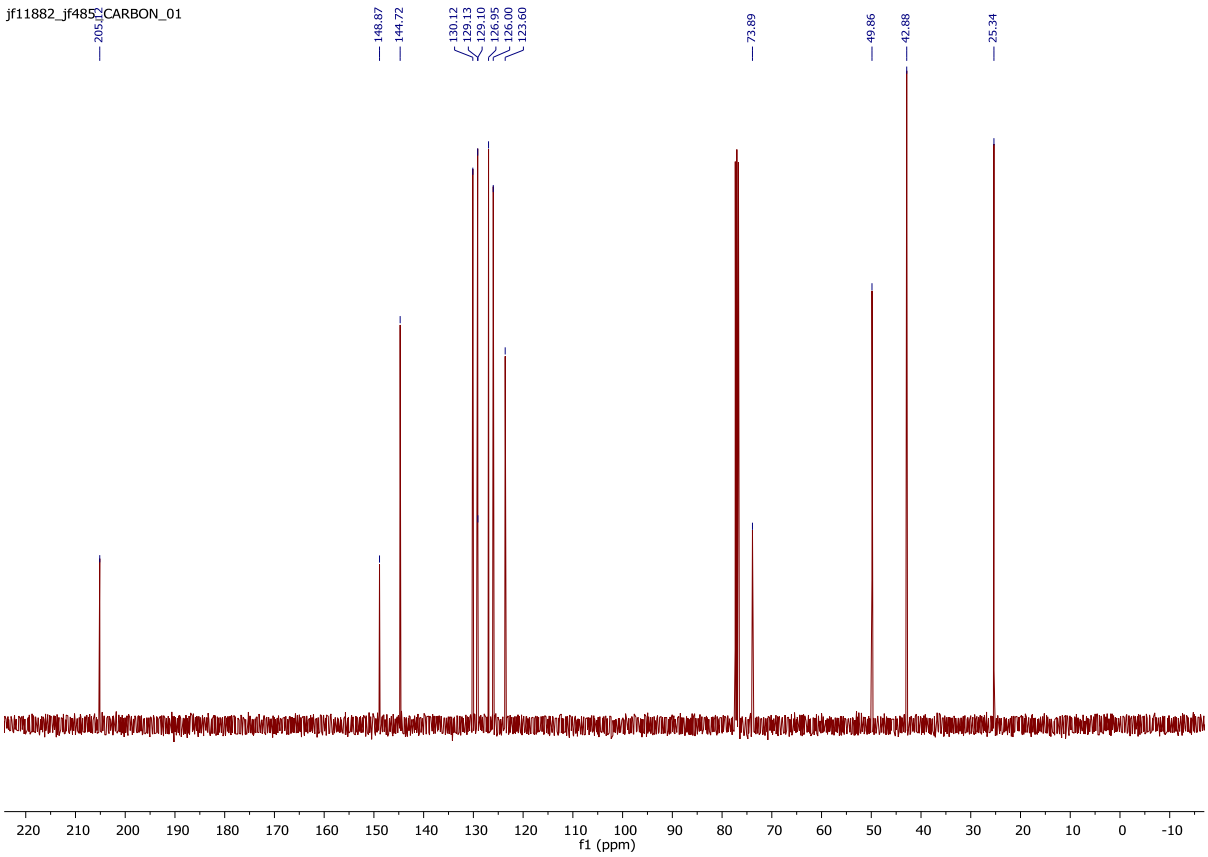
tert-butyl (3-(2-hydroxynaphthalen-1-yl)propyl)(tosyloxy)carbamate (5n)



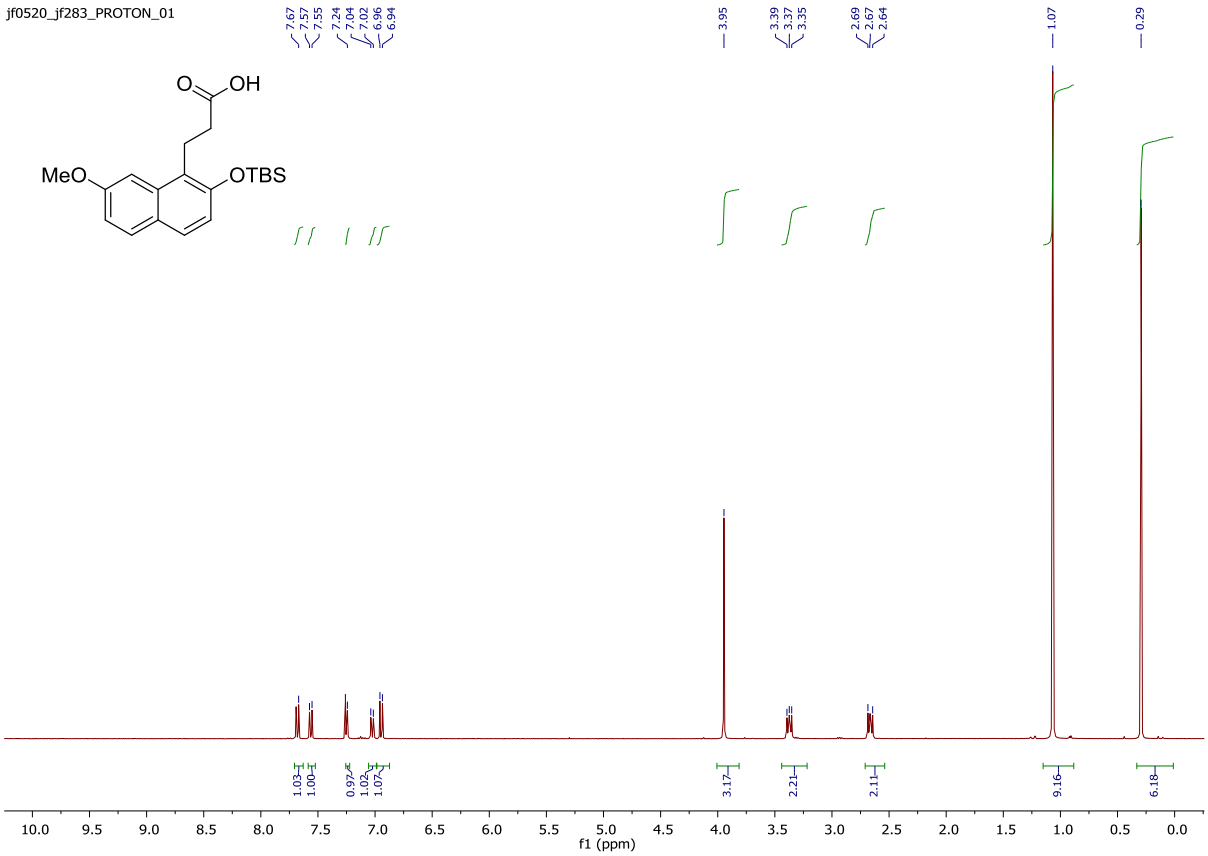


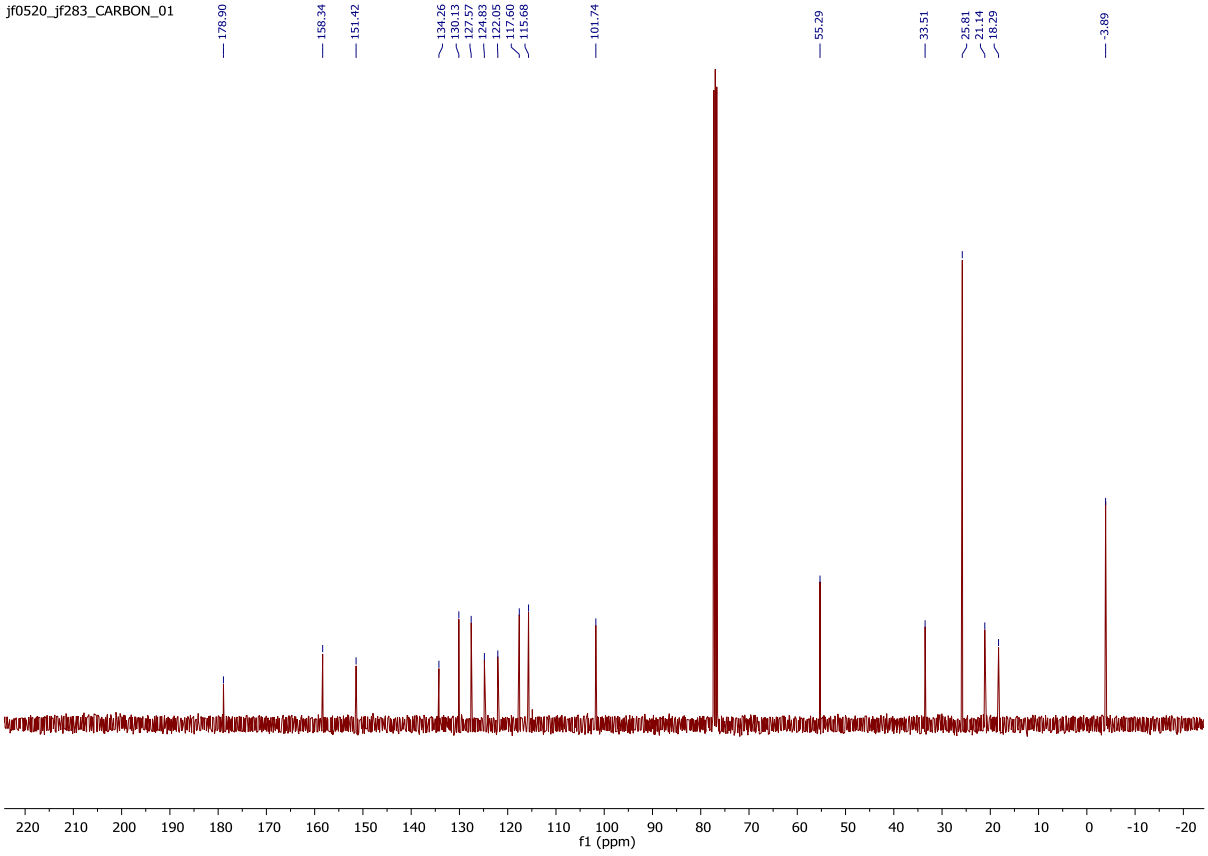
2*H*-spiro[naphthalene-1,2'-pyrrolidin]-2-one (7n)



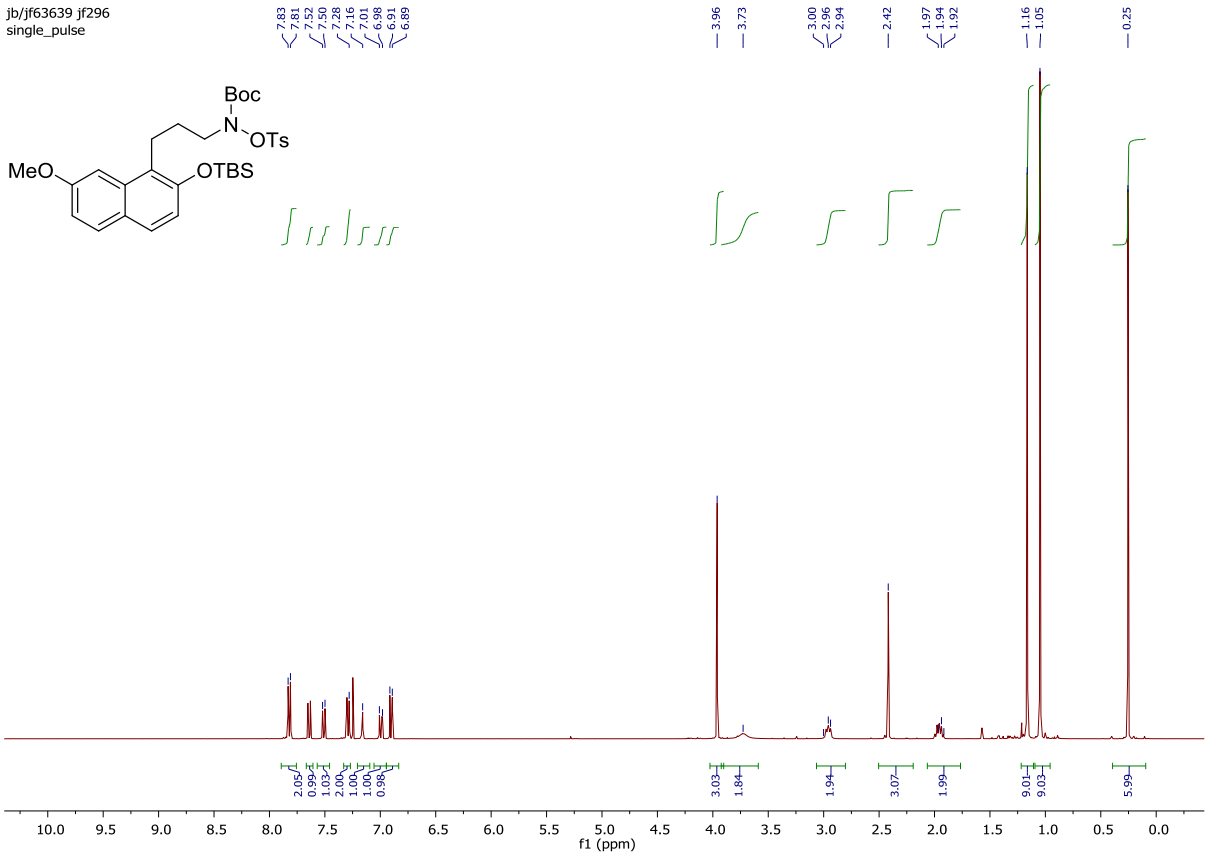


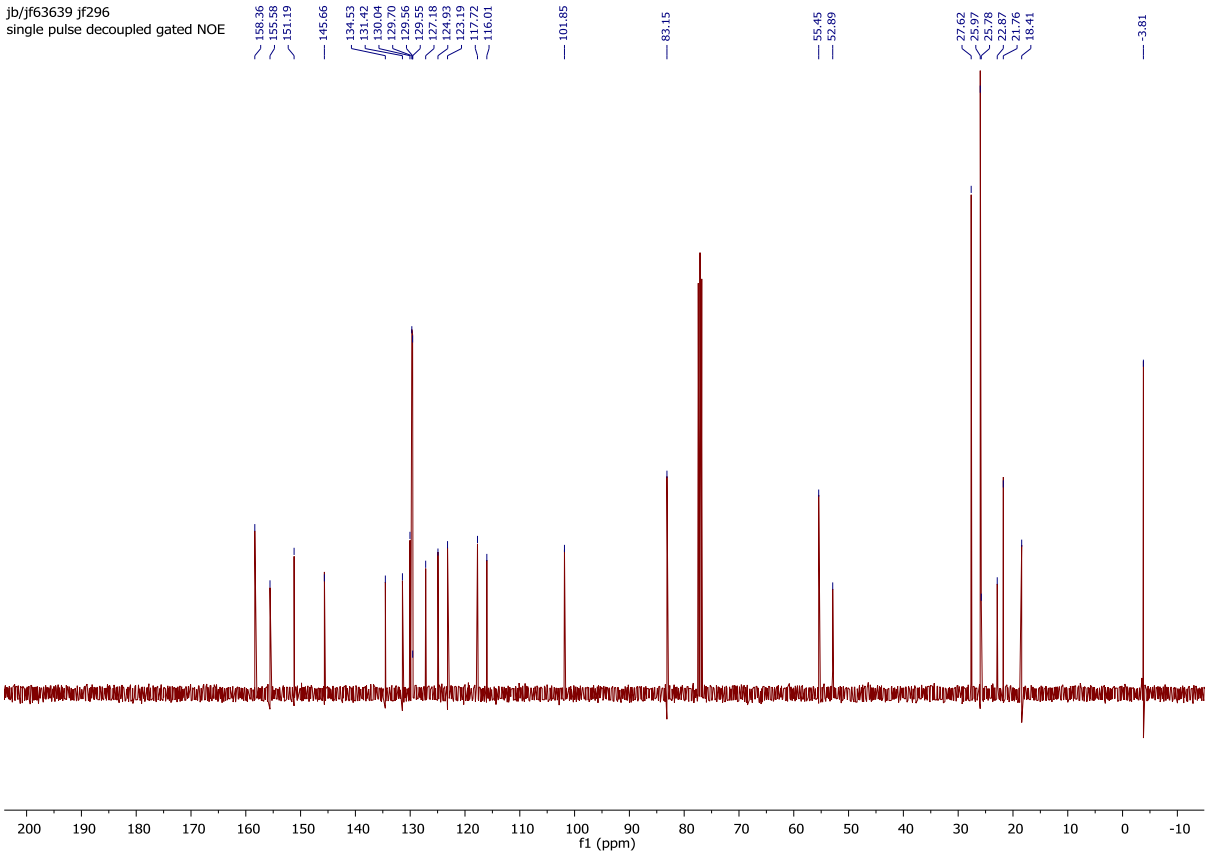
3-(2-((*tert*-Butyldimethylsilyl)oxy)-7-methoxynaphthalen-1-yl)propanoic acid



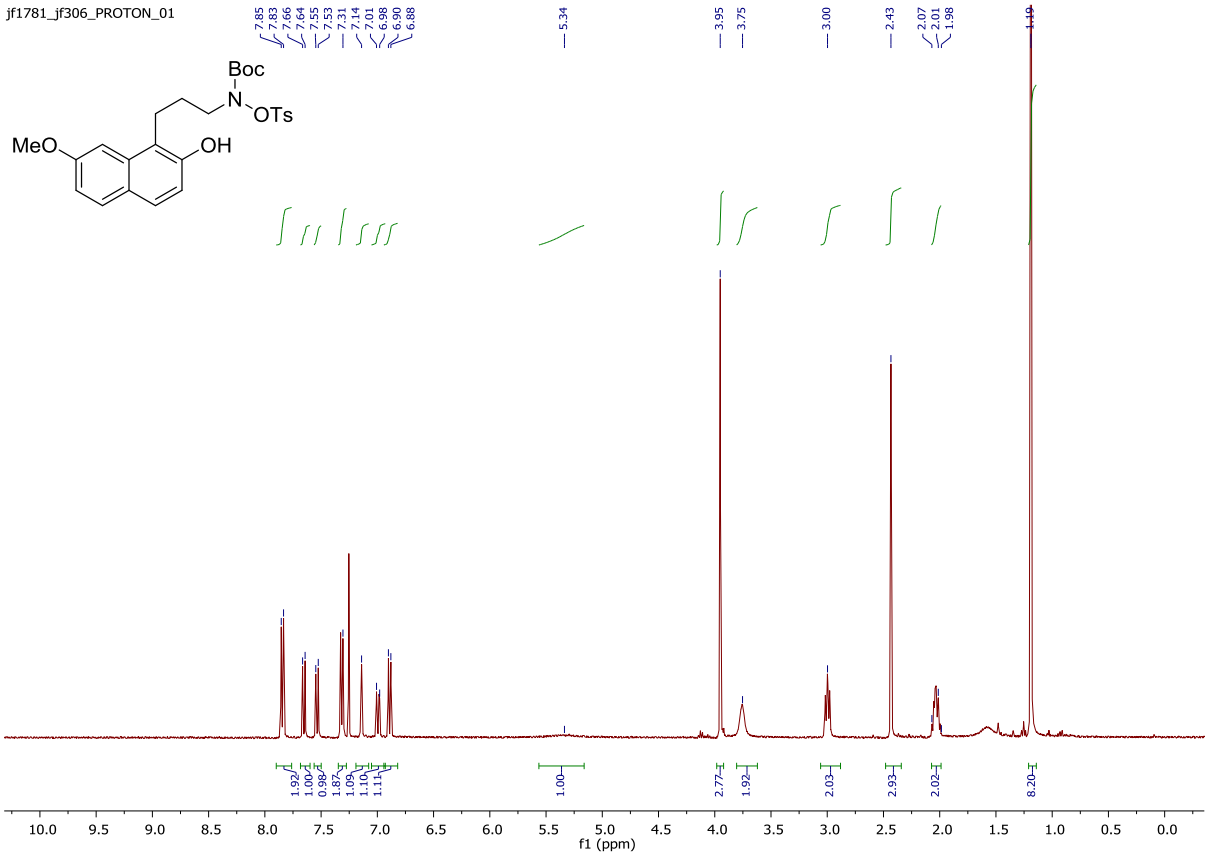


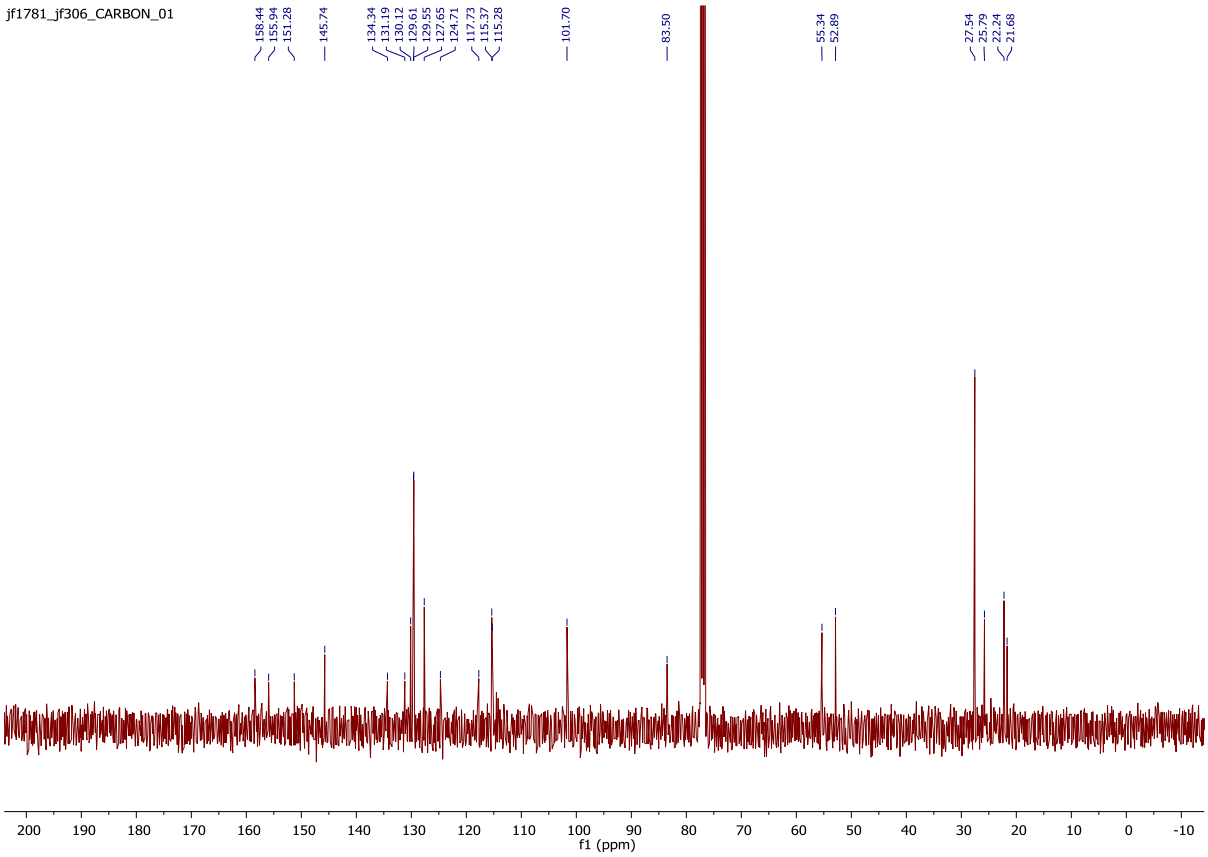
tert-Butyl (2-(2-((_tert_-butyldimethylsilyl)oxy)-7-methoxynaphthalen-1-yl)ethyl)(tosyloxy)carbamate



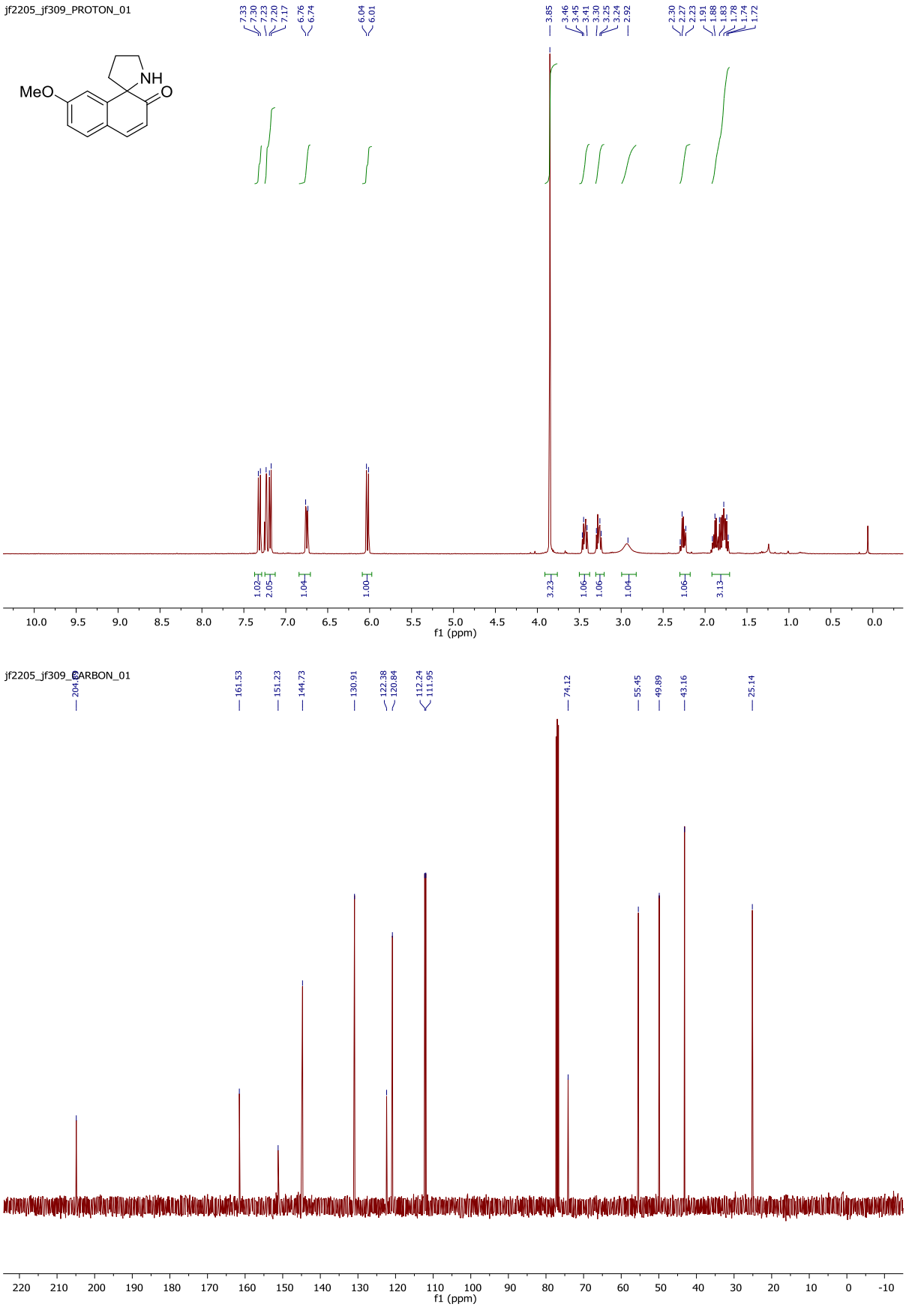


tert-Butyl (3-(2-hydroxy-7-methoxynaphthalen-1-yl)propyl)(tosyloxy)carbamate (5o)

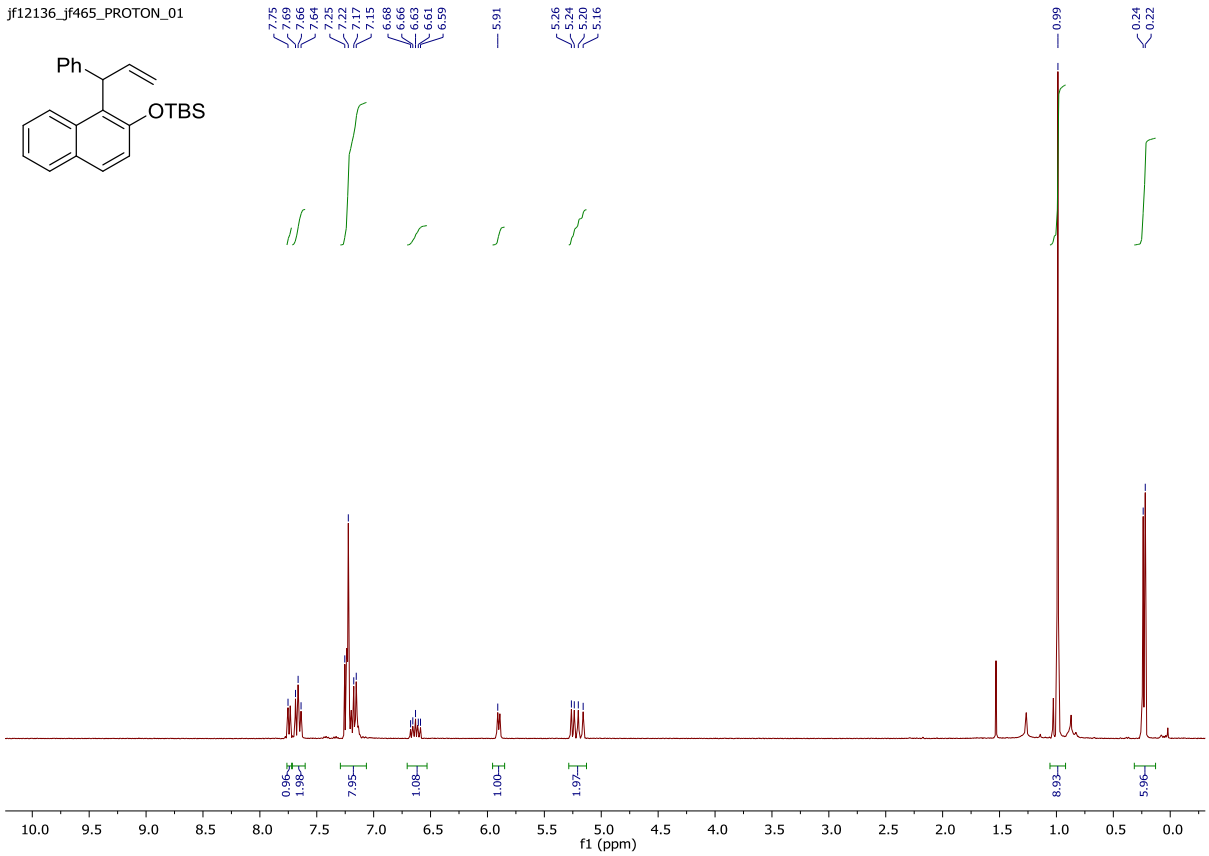


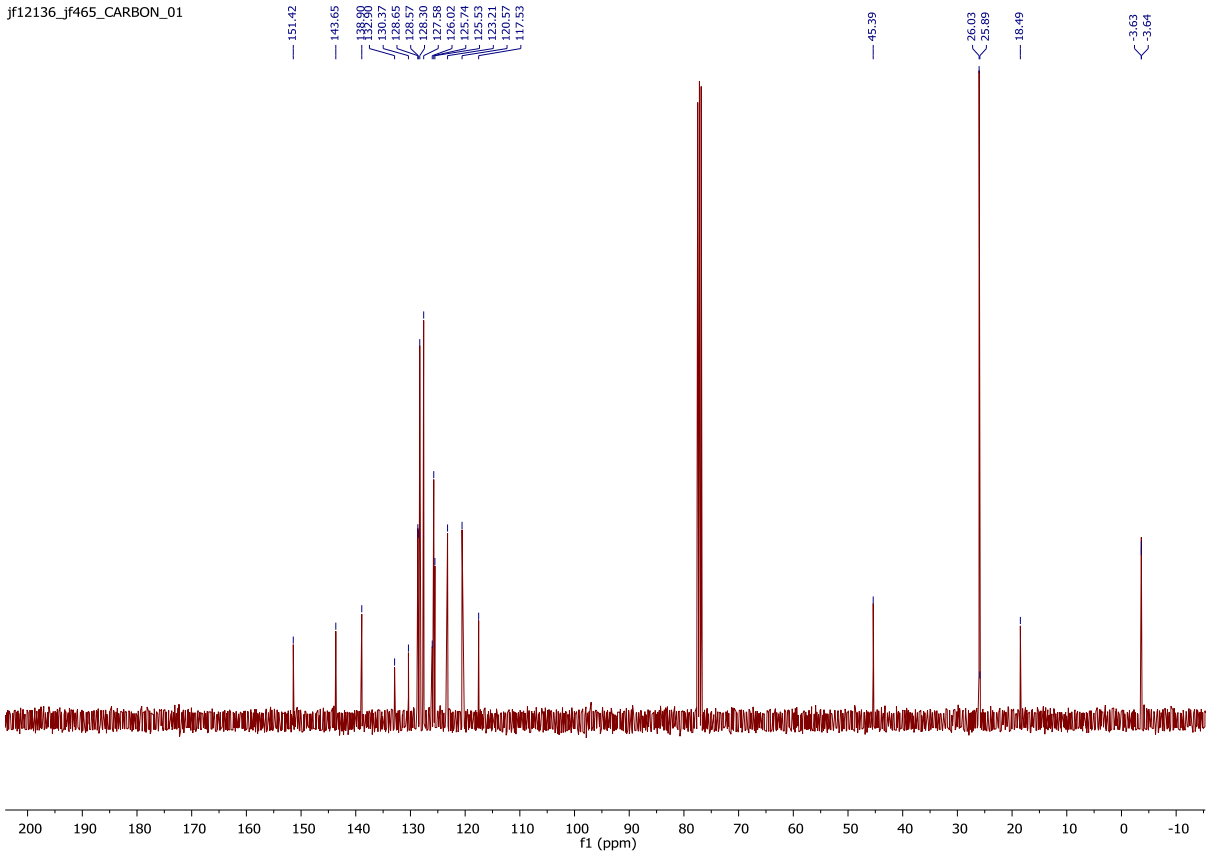


7-methoxy-2*H*-spiro[naphthalene-1,2'-pyrrolidin]-2-one (7o)

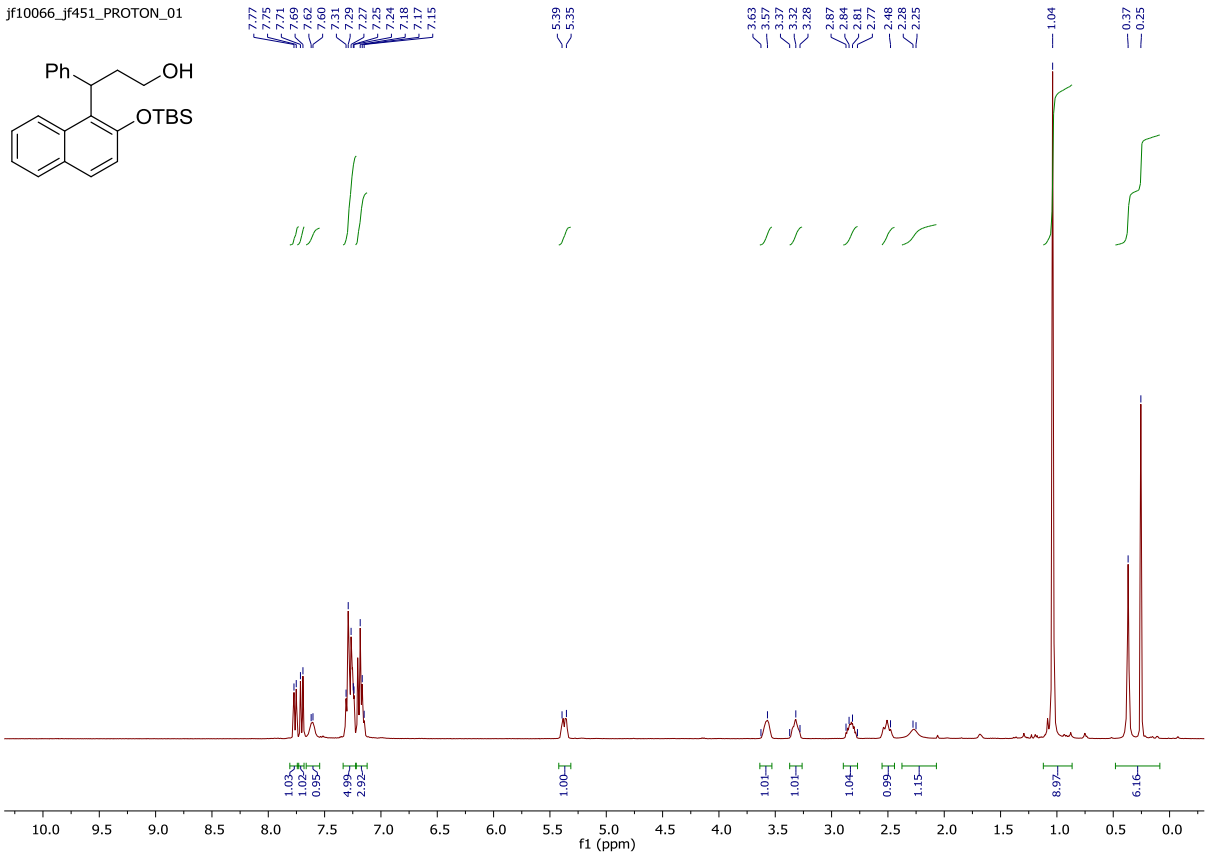


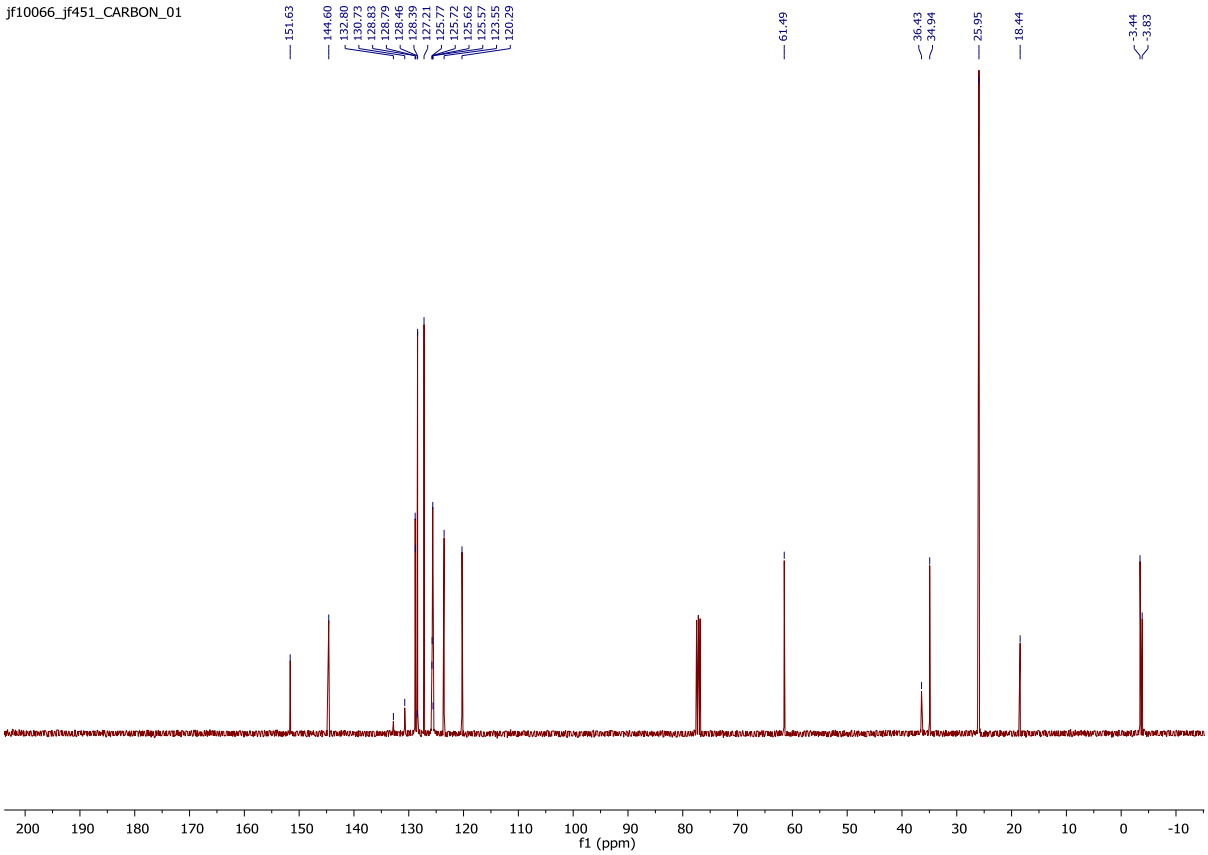
tert-Butyldimethyl((1-(1-phenylallyl)naphthalen-2-yl)oxy)silane



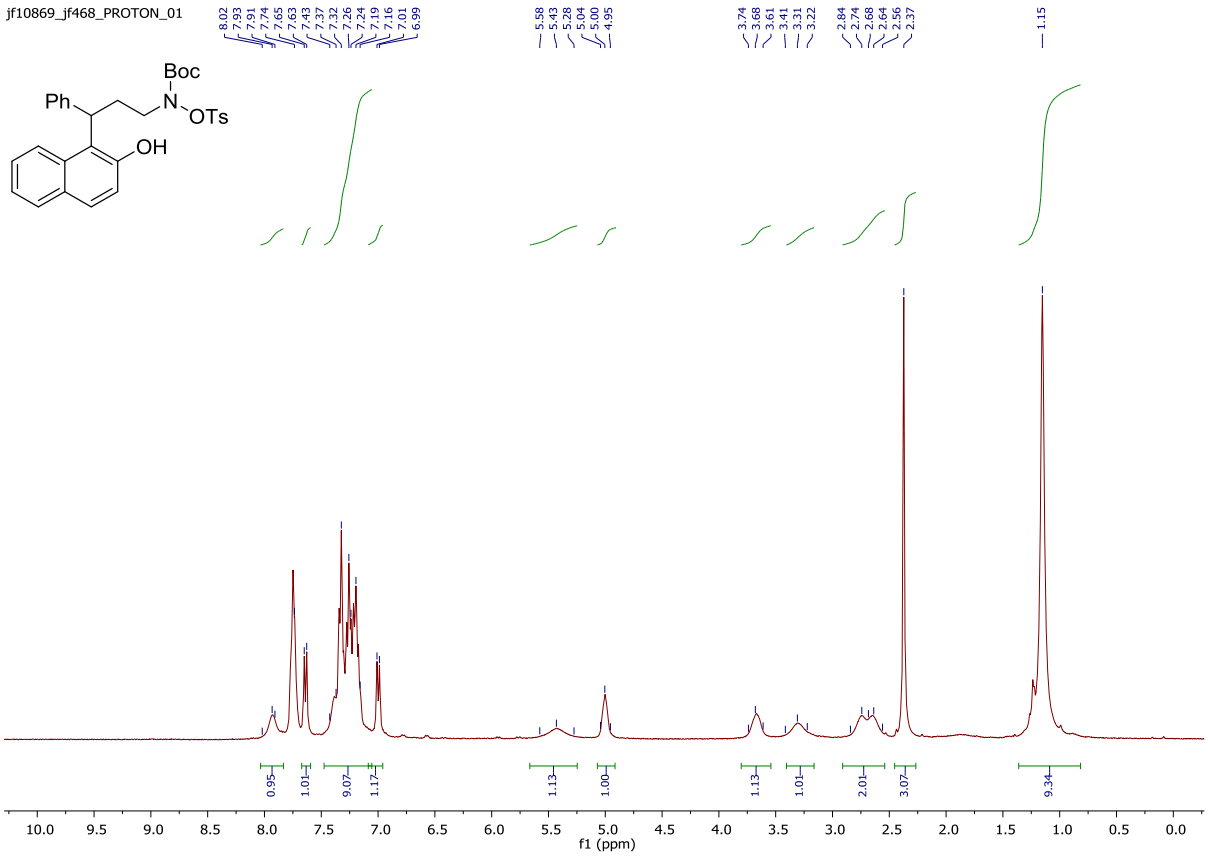


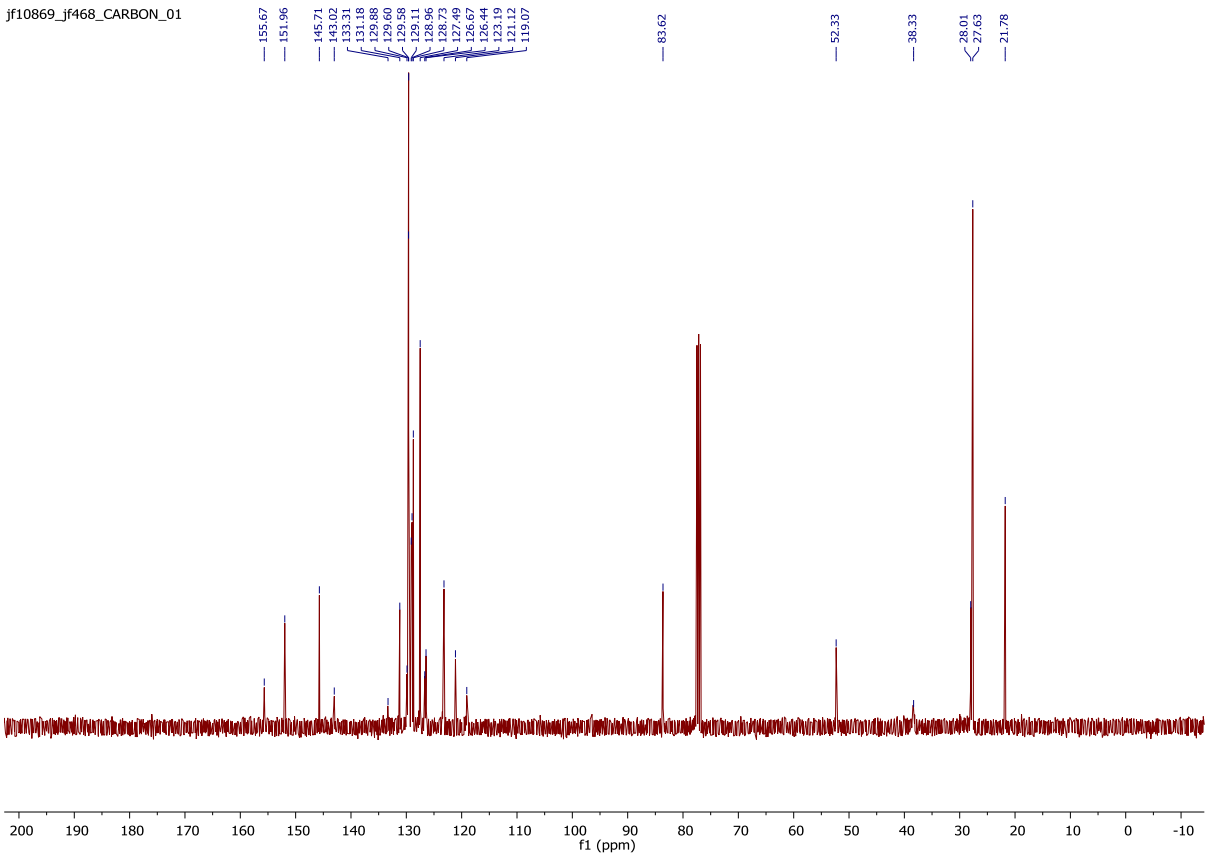
3-(2-((*tert*-Butyldimethylsilyl)oxy)naphthalen-1-yl)-3-phenylpropan-1-ol



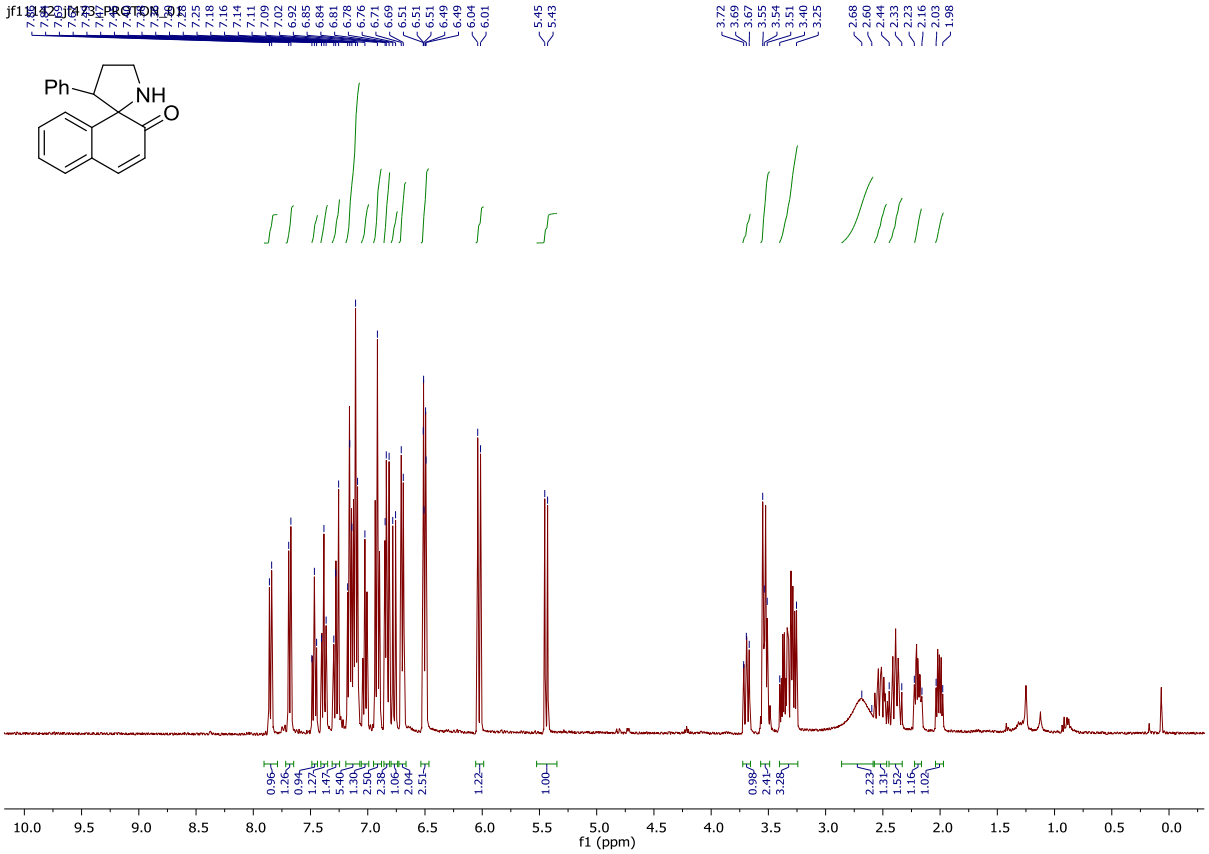


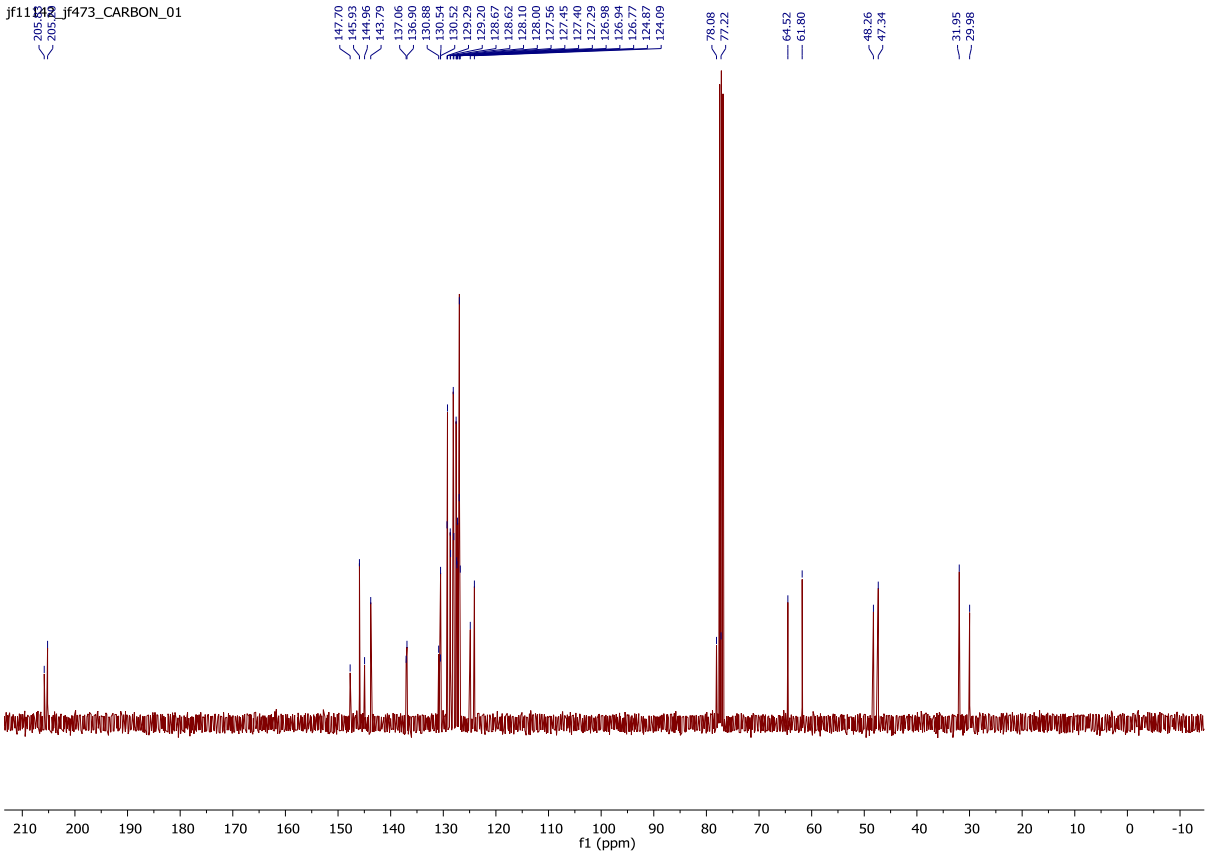
tert-Butyl (3-(2-hydroxynaphthalen-1-yl)-3-phenylpropyl)(tosyloxy)carbamate (5p)



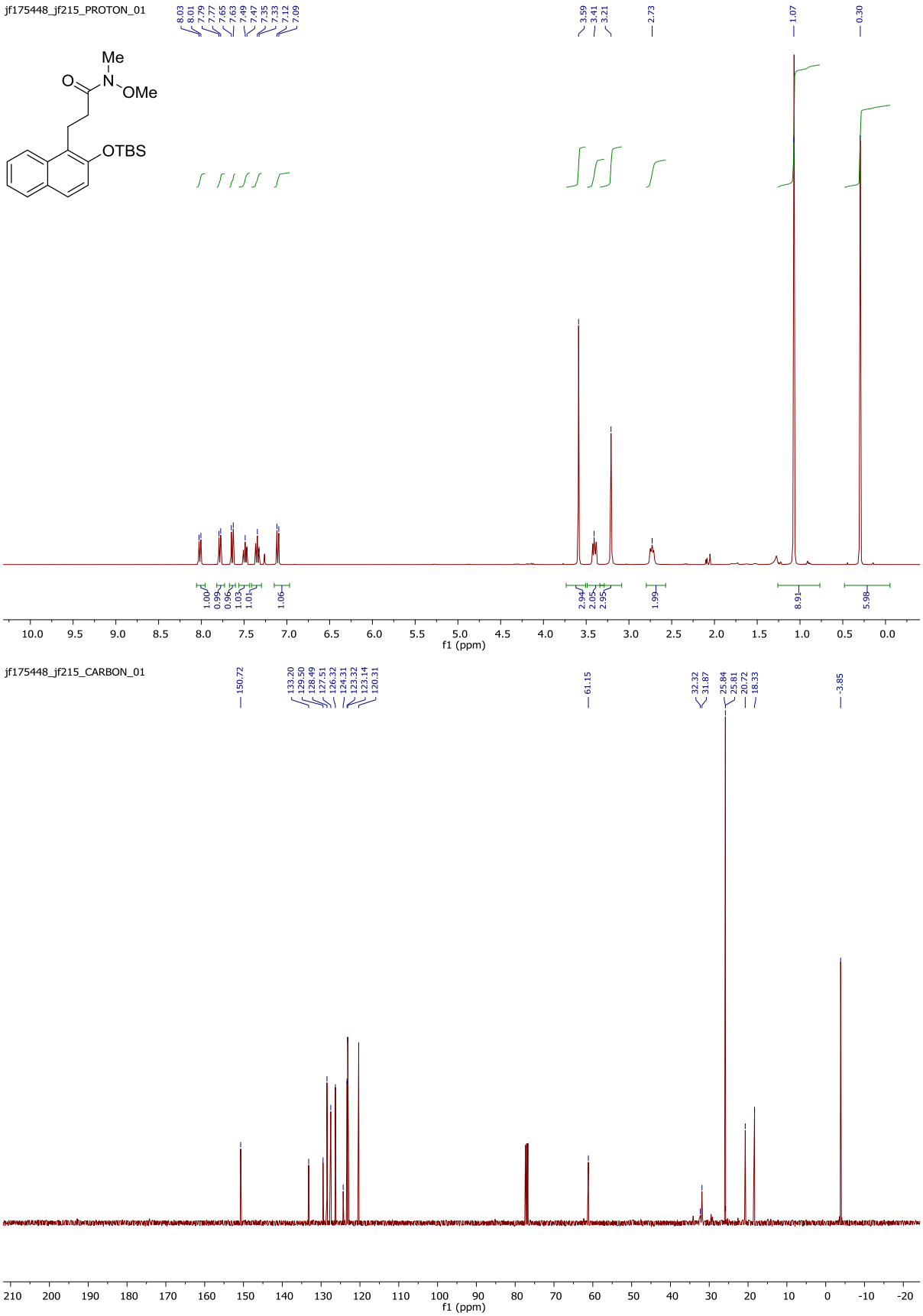


3'-phenyl-2*H*-spiro[naphthalene-1,2'-pyrrolidin]-2-one (7p)

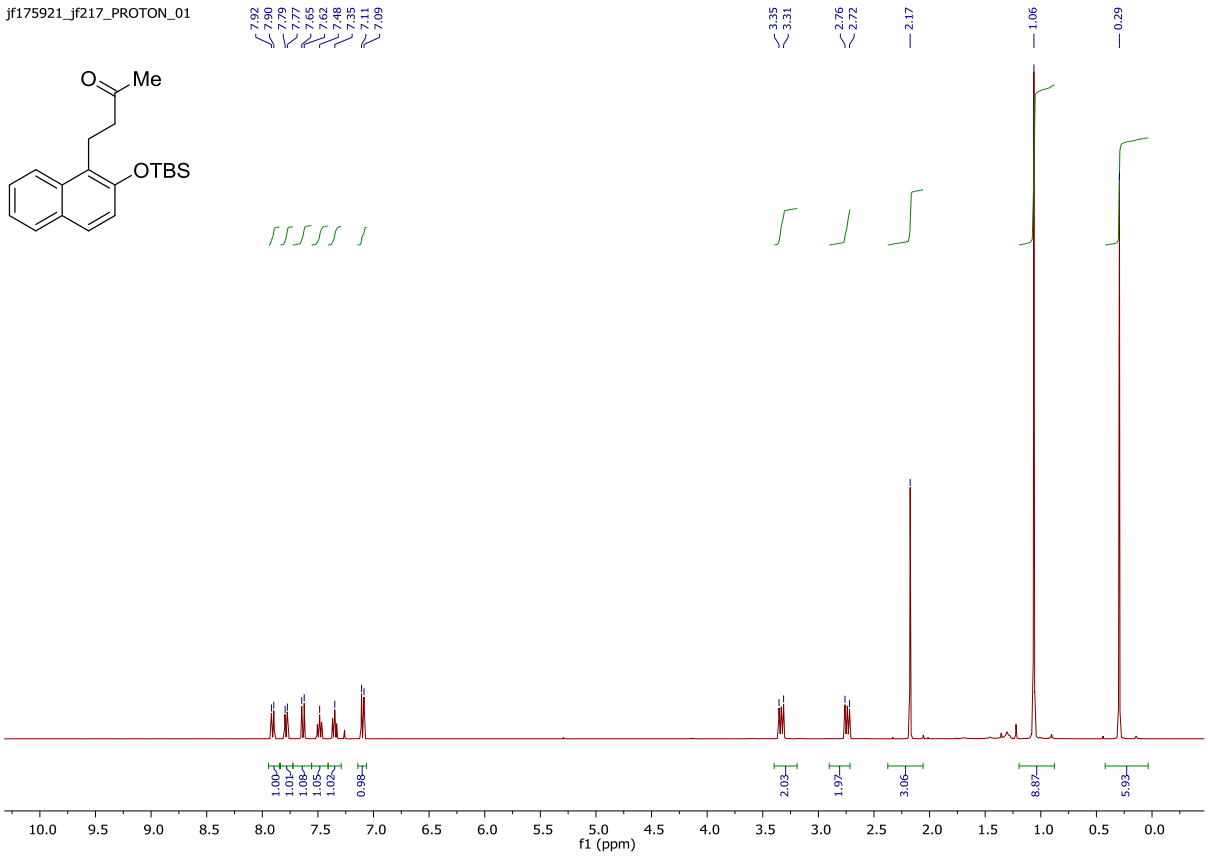


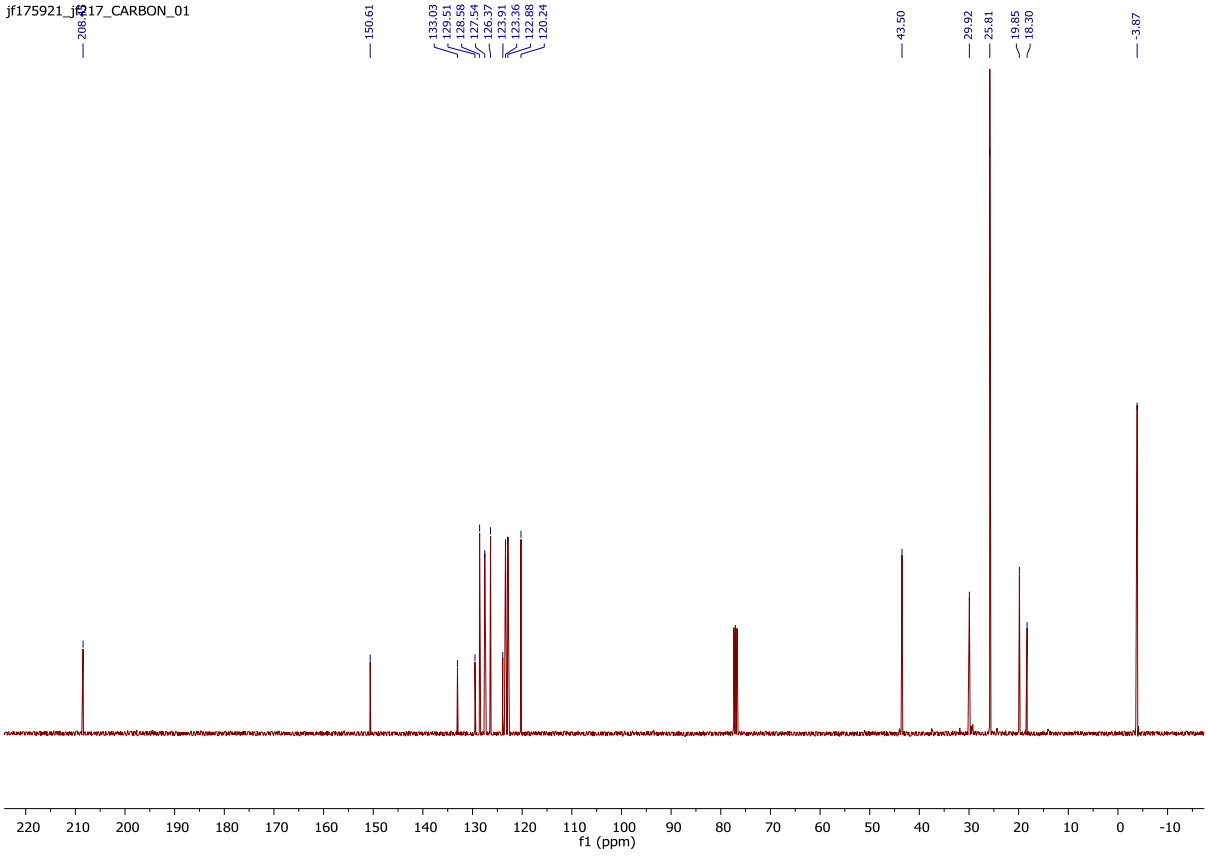


3-(2-((*tert*-Butyldimethylsilyl)oxy)naphthalen-1-yl)-*N*-methoxy-*N*-methylpropanamide

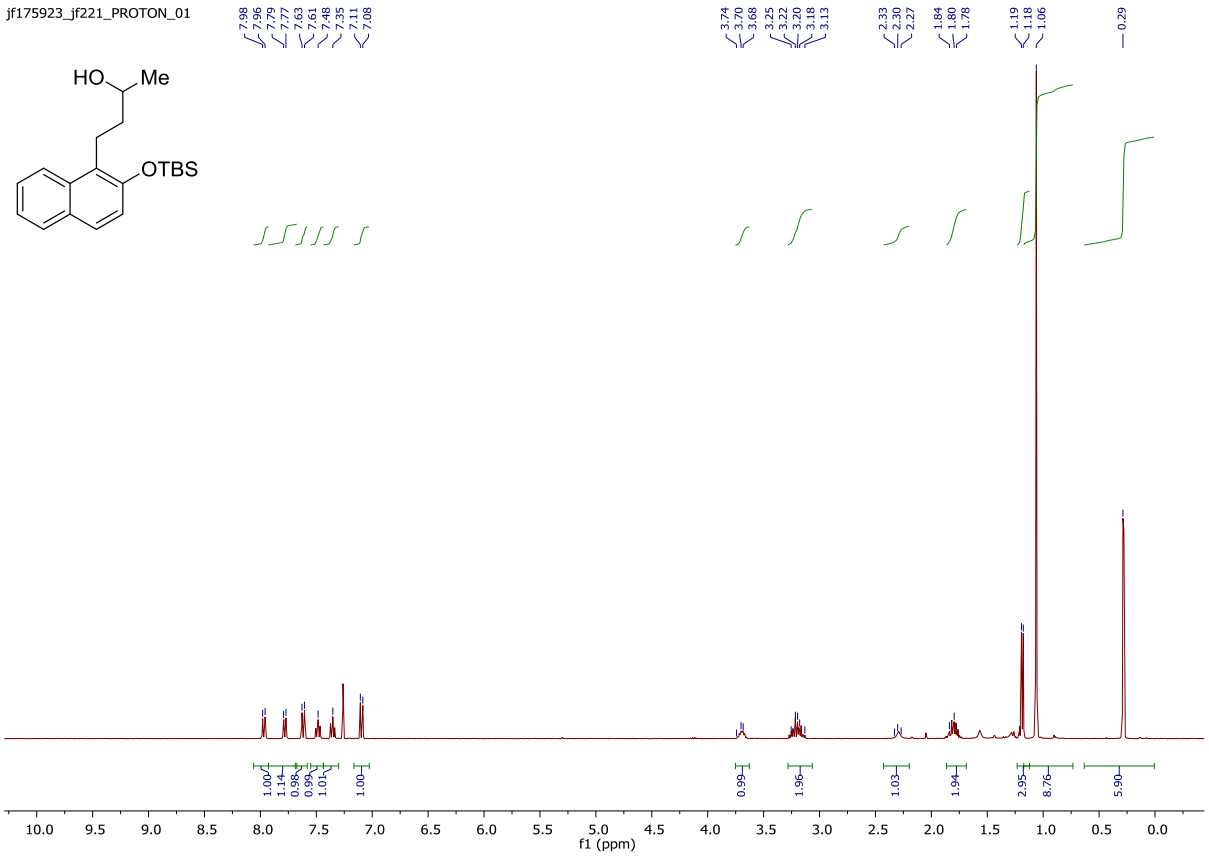


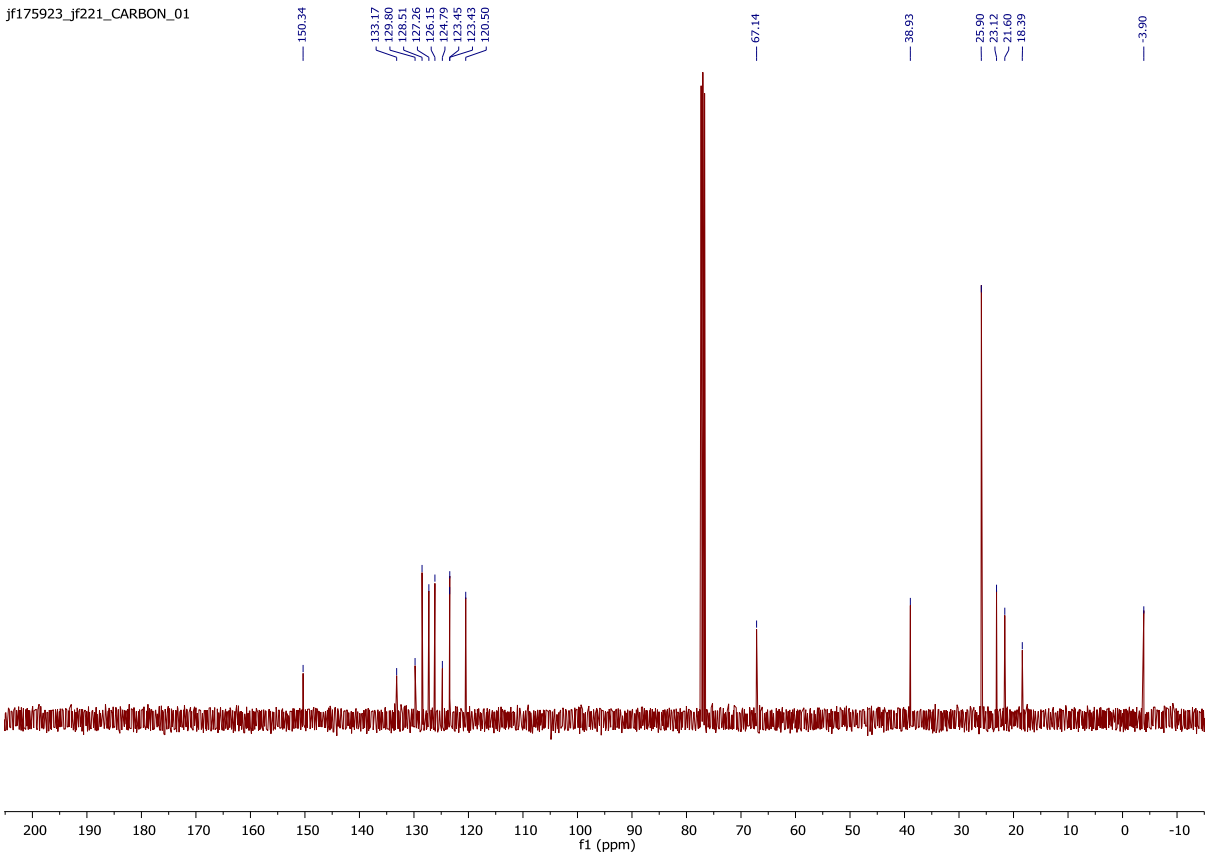
4-(2-((*tert*-Butyldimethylsilyl)oxy)naphthalen-1-yl)butan-2-one



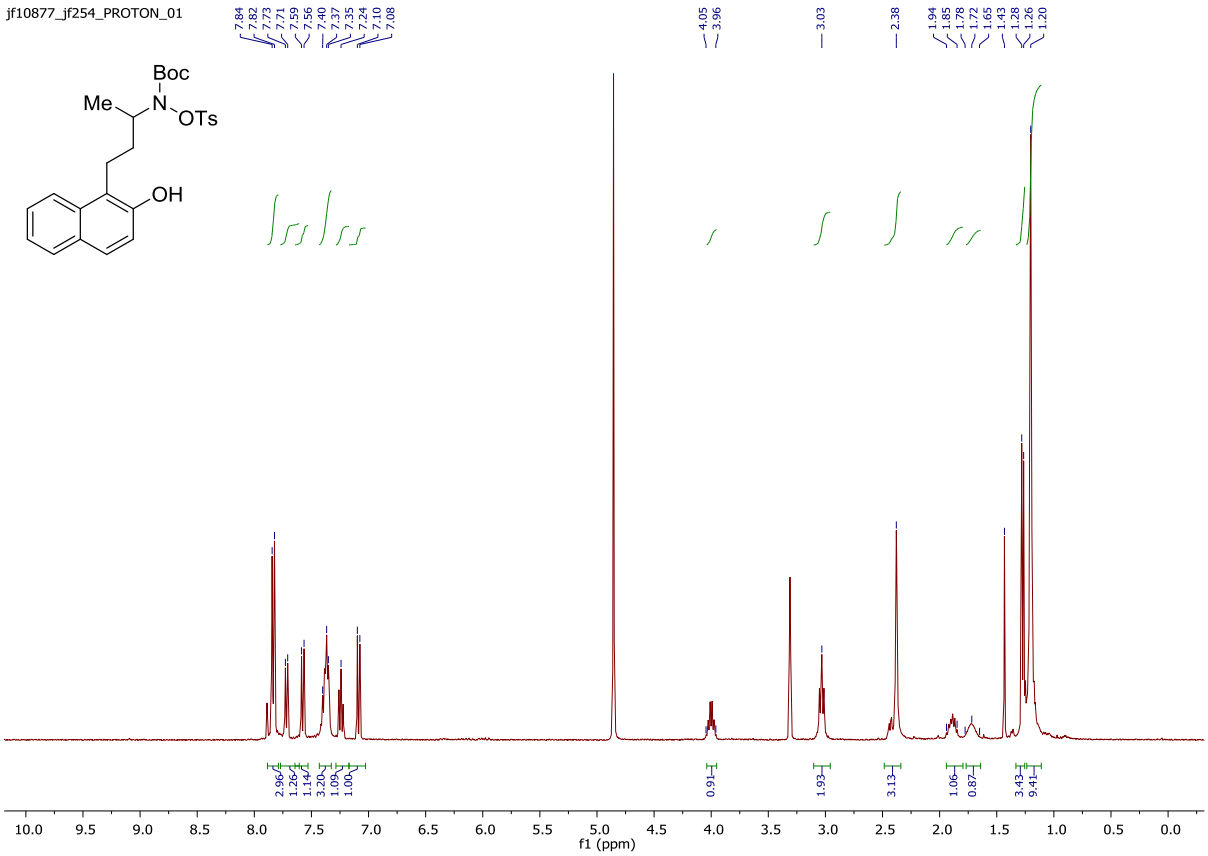


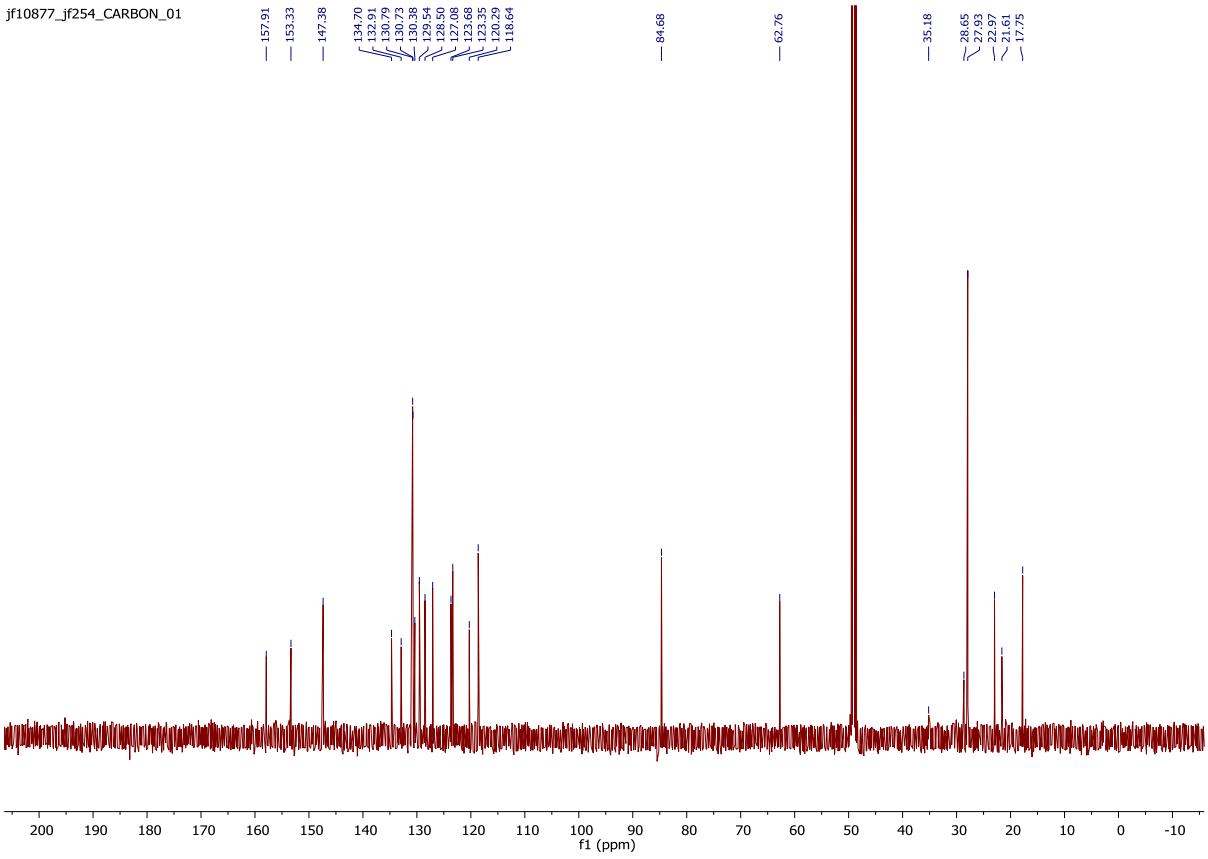
4-(2-((*tert*-Butyldimethylsilyl)oxy)naphthalen-1-yl)butan-2-ol



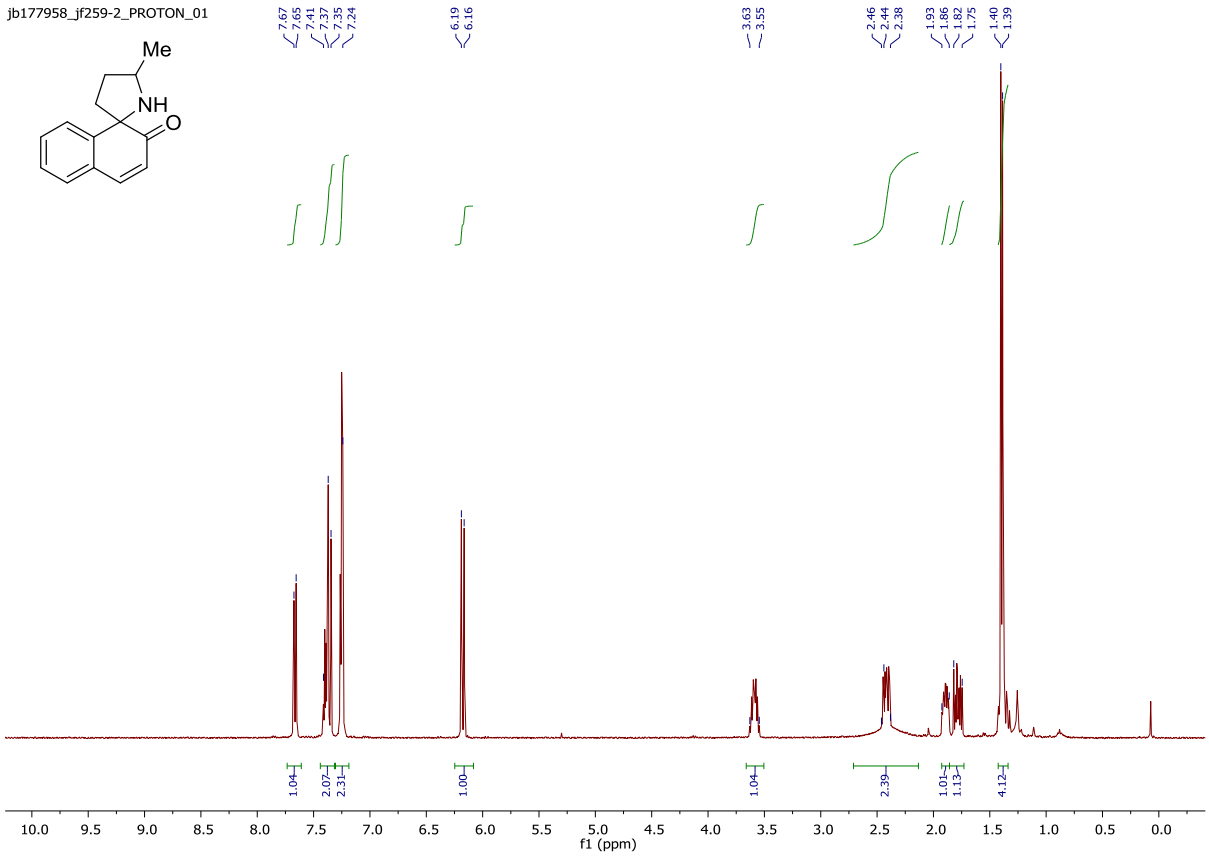


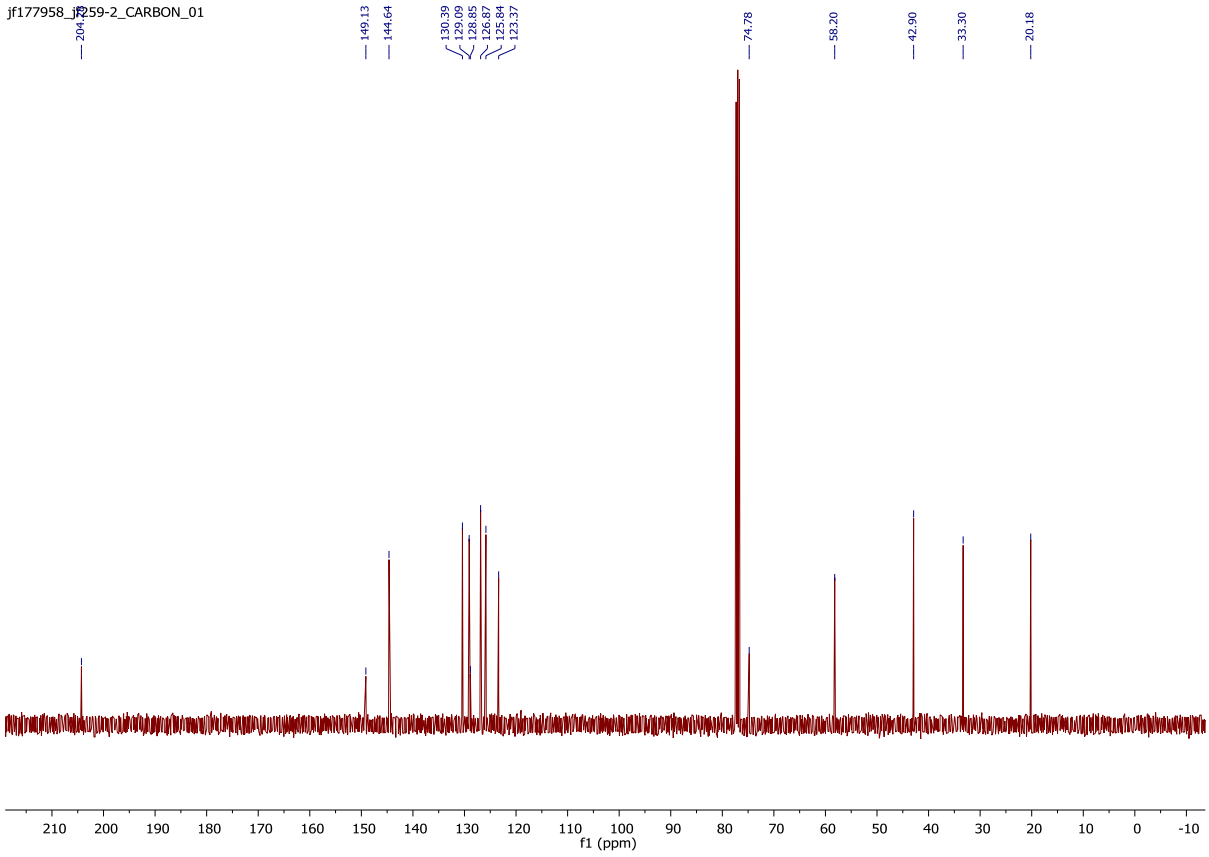
tert-Butyl (4-(2-hydroxynaphthalen-1-yl)butan-2-yl)(tosyloxy)carbamate (5q)



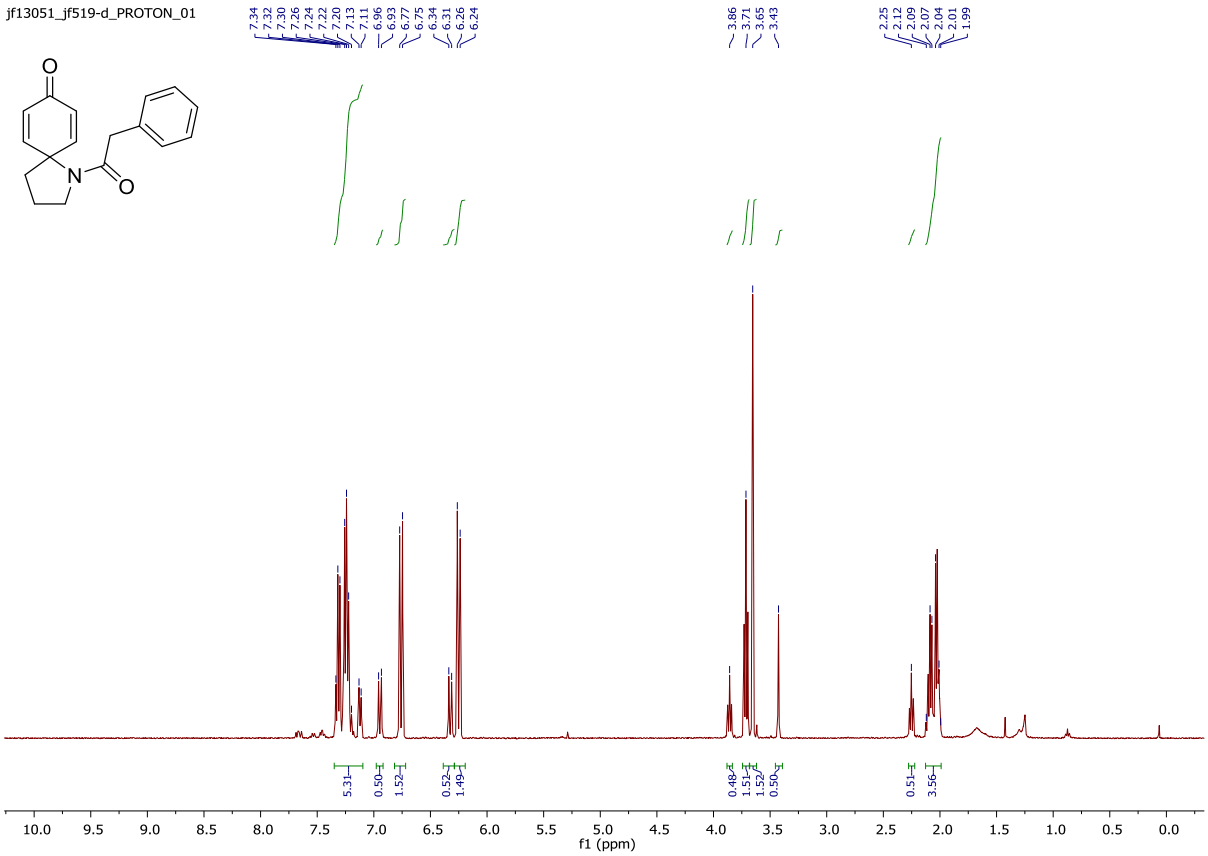


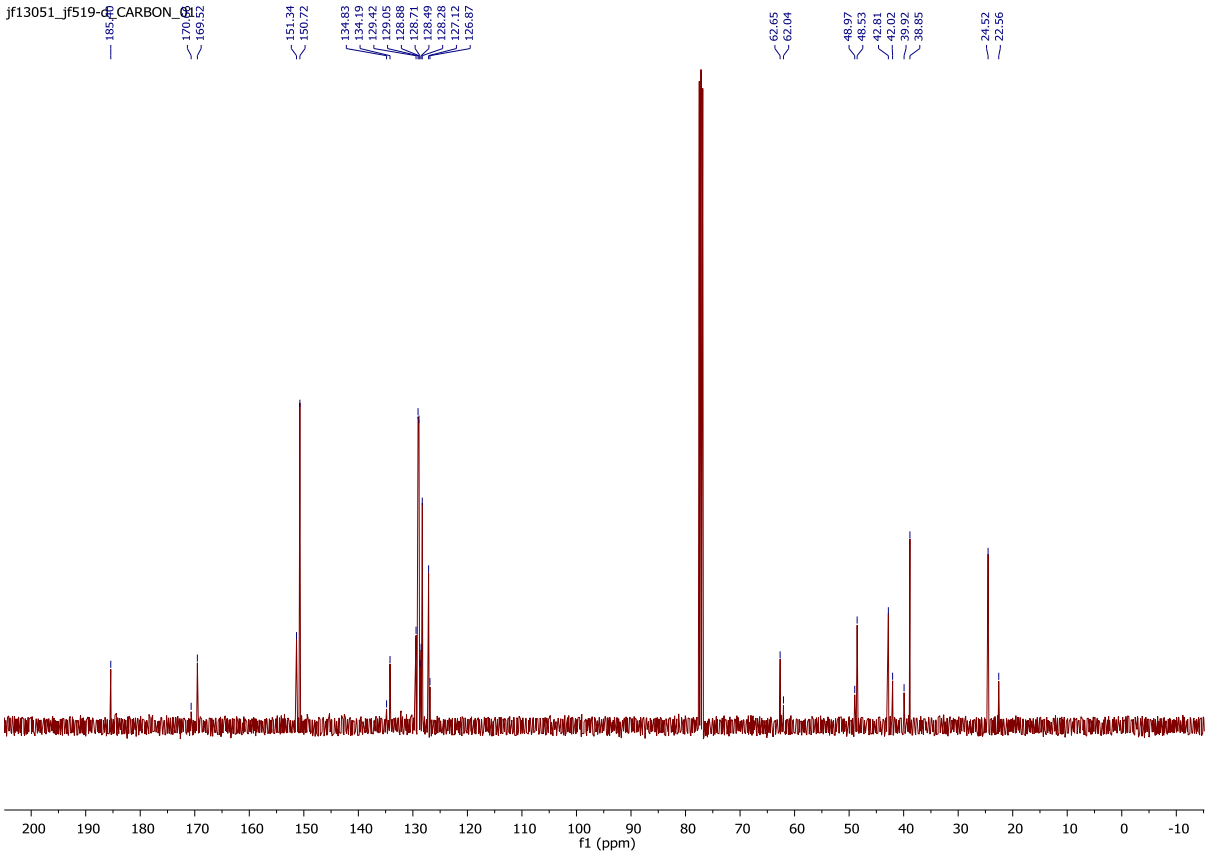
5'-Methyl-2*H*-spiro[naphthalene-1,2'-pyrrolidin]-2-one (7q)



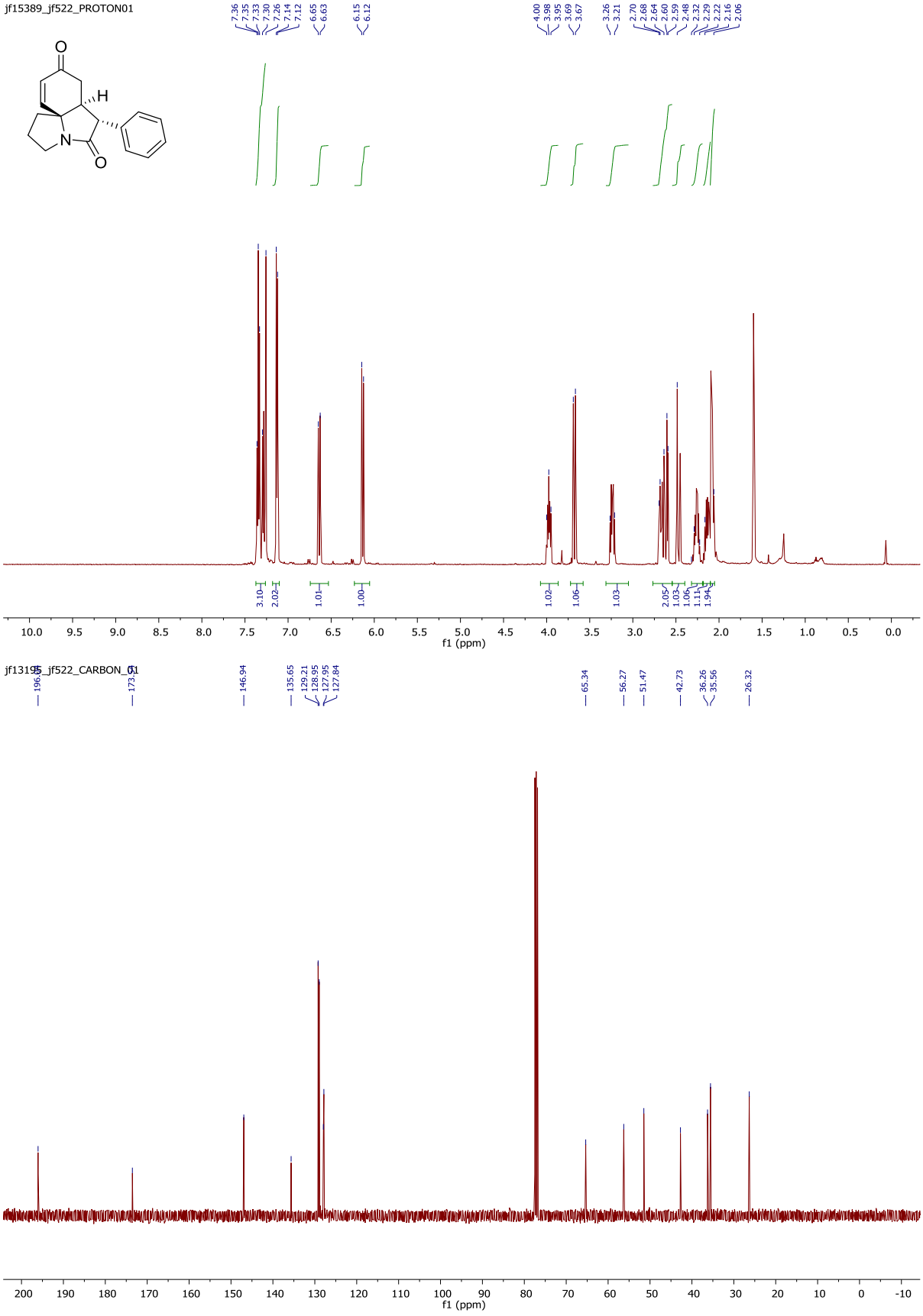


1-(2-Phenylacetyl)-1-azaspiro[4.5]deca-6,9-dien-8-one (9a)

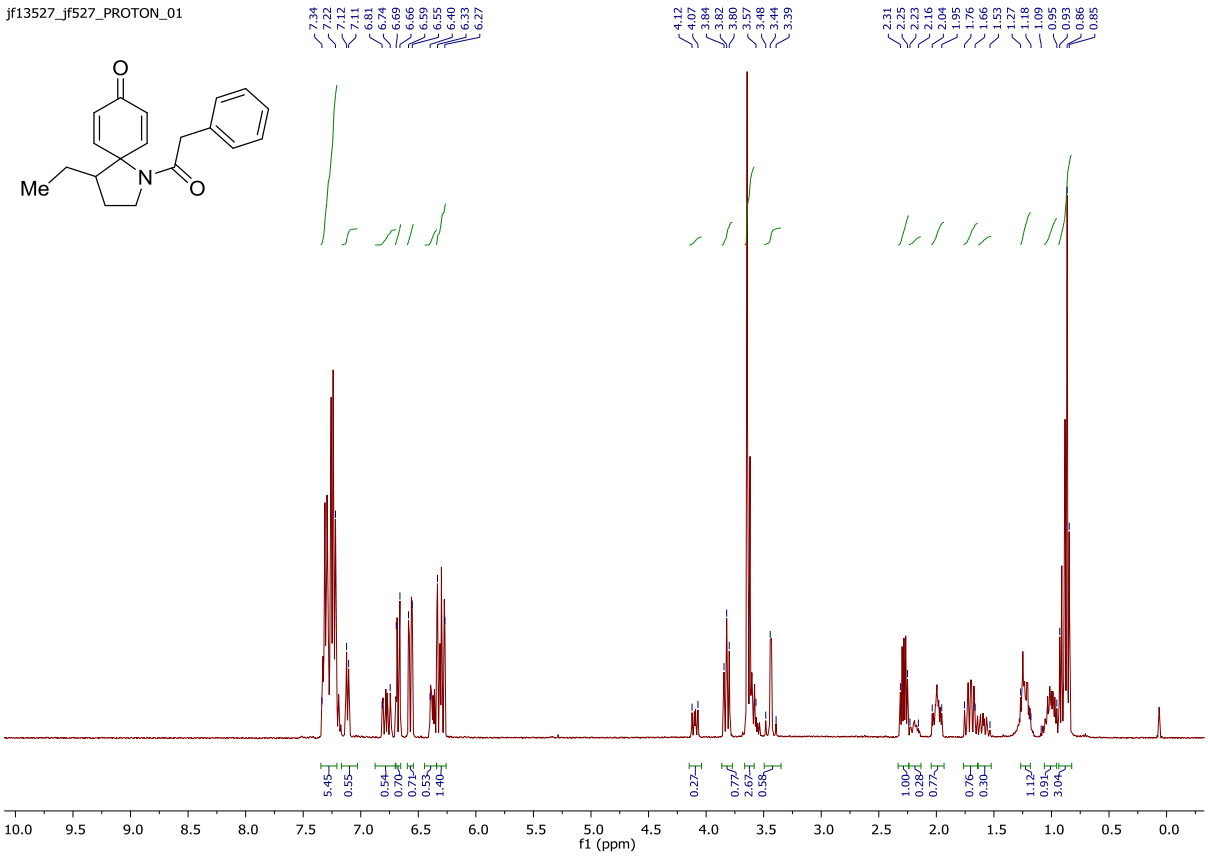


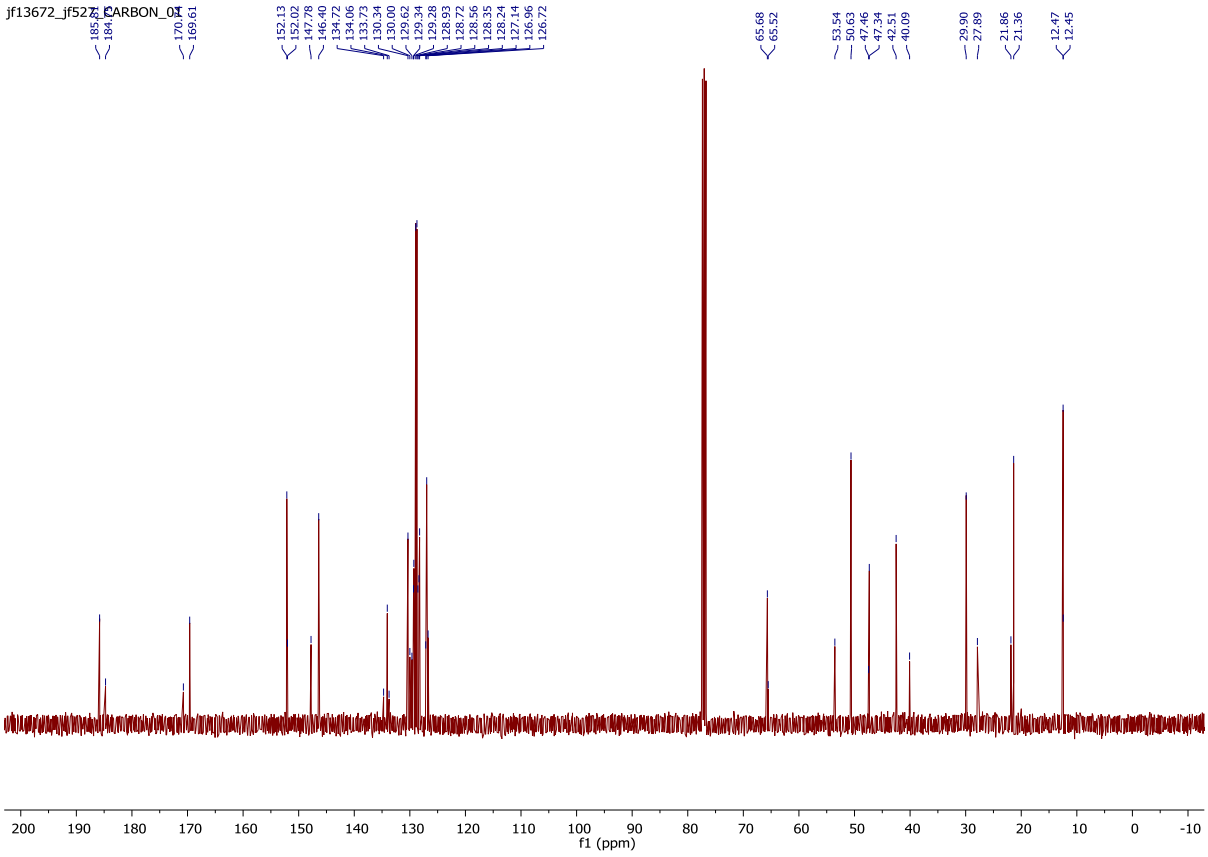


(6*R, 6a*S**, 10a*S**)-6-phenyl-2,3,6a,7-tetrahydro-1*H*,5*H*-pyrrolo[2,1-*i*]indole-5,8(6*H*)-dione (10a)**

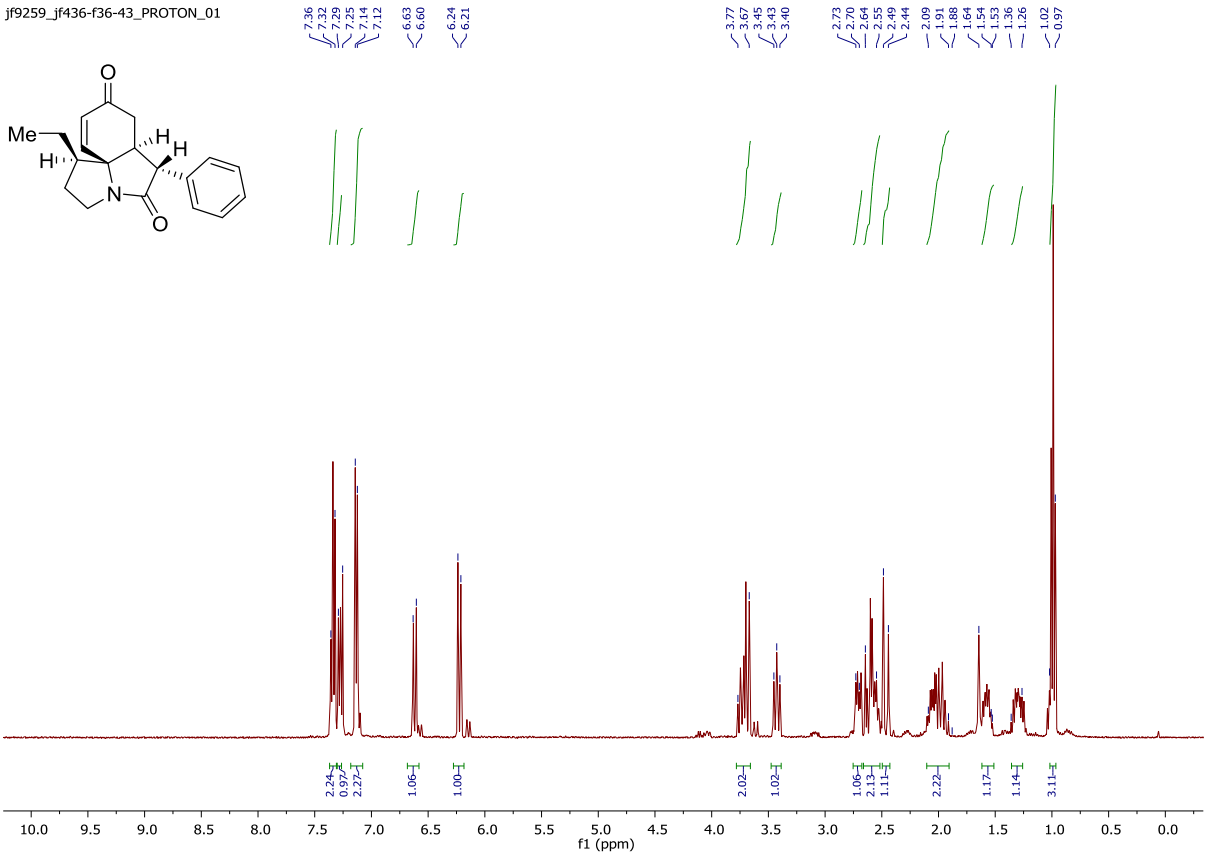


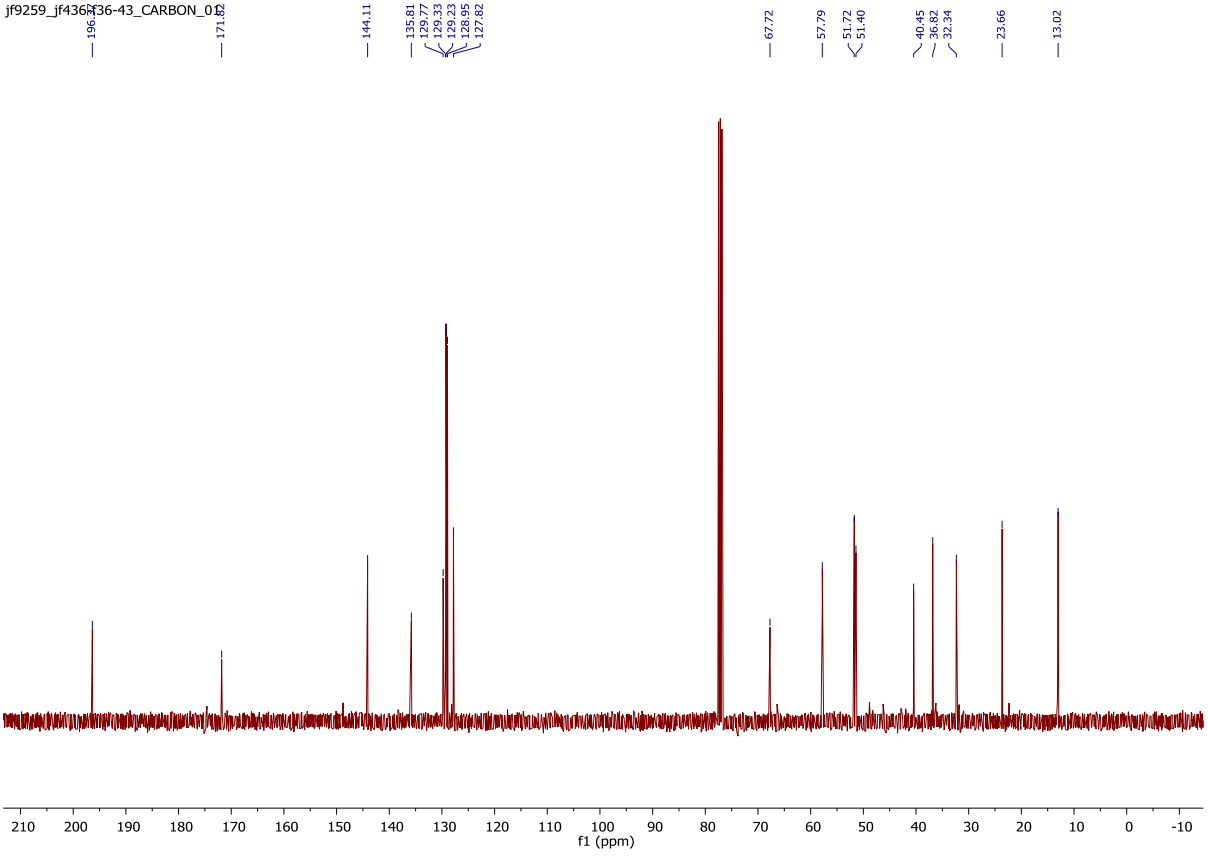
4-Ethyl-1-(2-phenylacetyl)-1-azaspiro[4.5]deca-6,9-dien-8-one (9g)



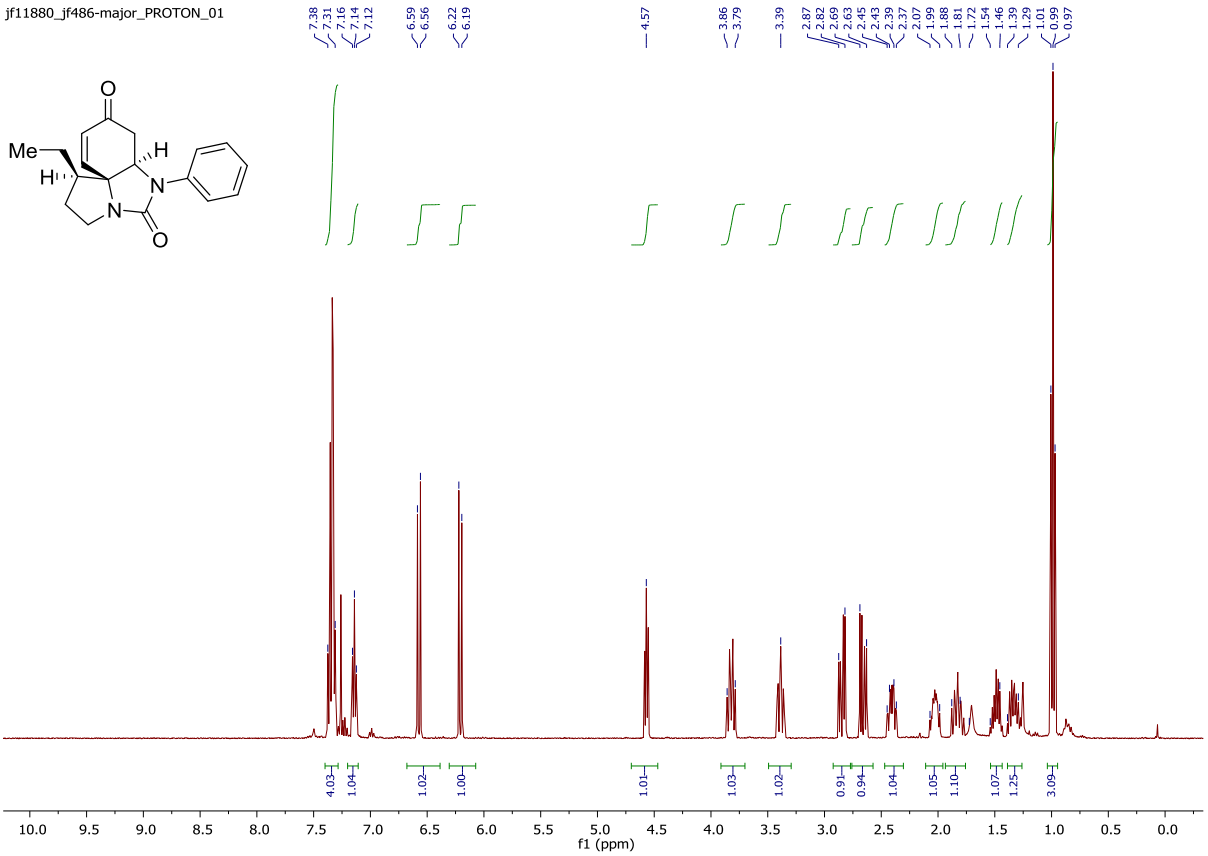


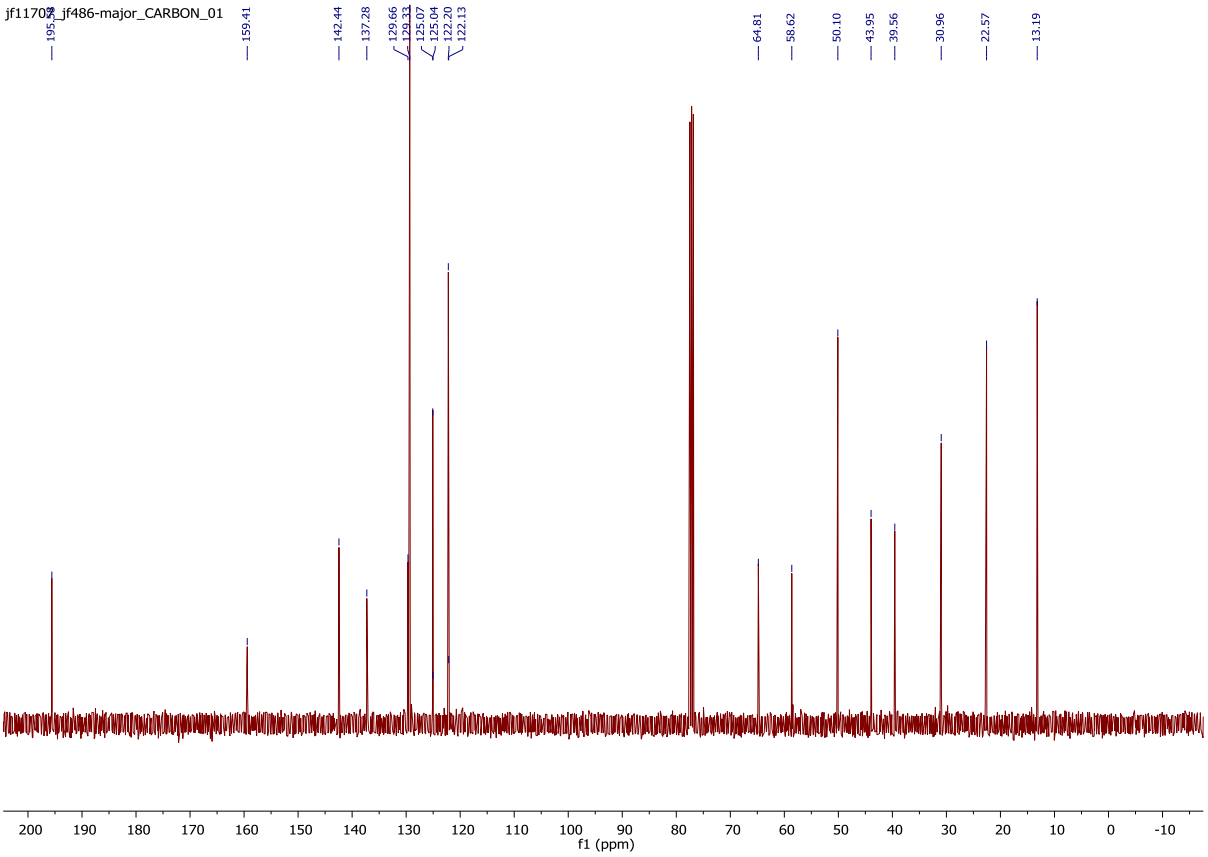
(1*R, 6*R**, 6a*S**, 10a*S**)-1-Ethyl-6-phenyl-2,3,6a,7-tetrahydro-1*H*,5*H*-pyrrolo[2,1-i]indole-5,8(6*H*)-dione (10g)**



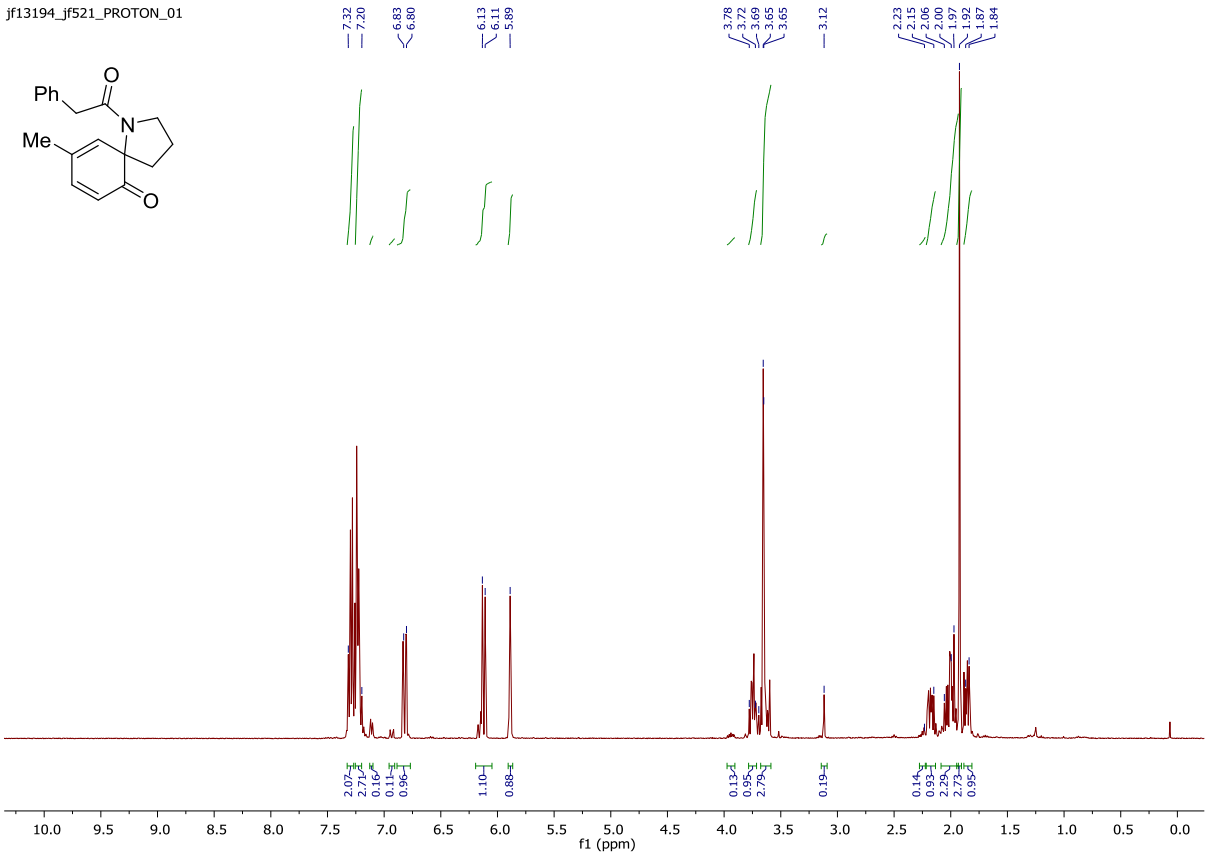


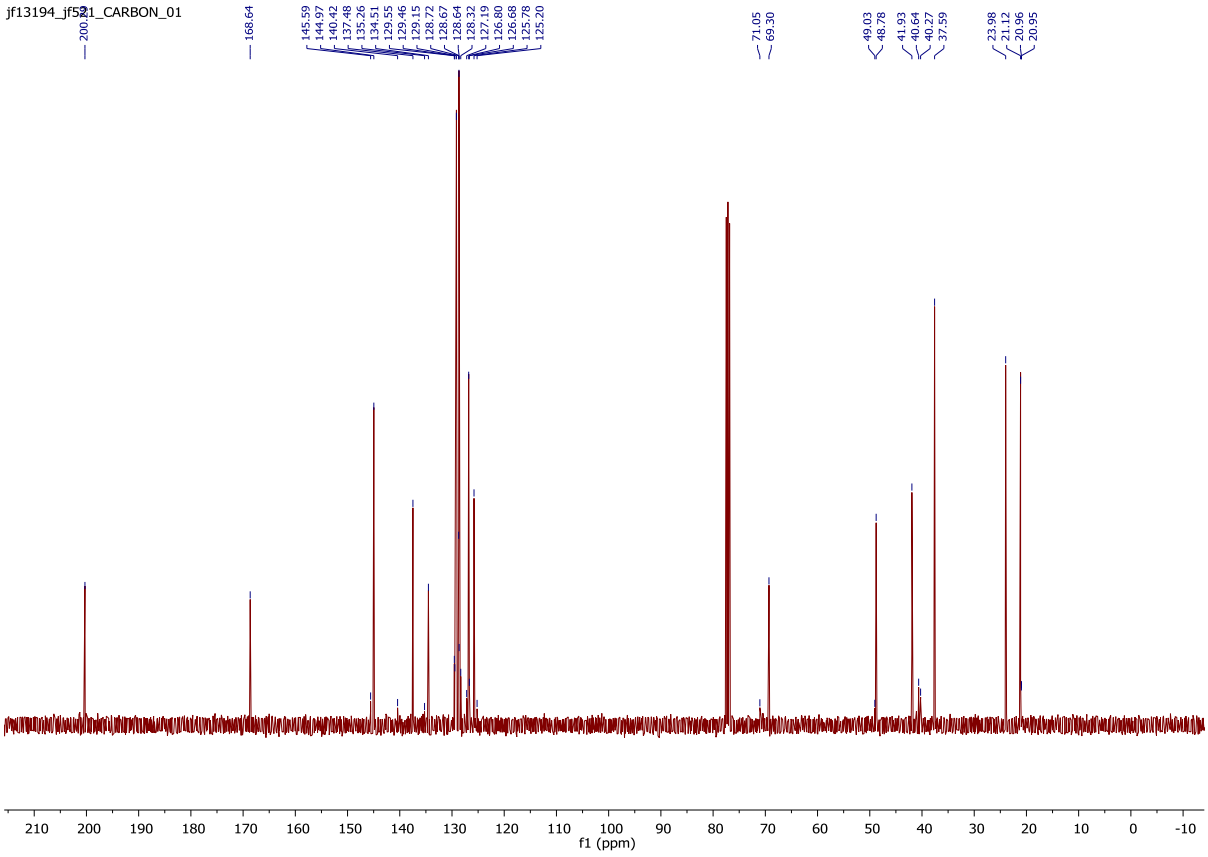
(1*R, 6a*R**, 10a*S**)-1-Ethyl-6-phenyl-2,3,6a,7-tetrahydro-1*H*,5*H*-benzo[d]pyrrolo[1,2-c]imidazole-5,8(6*H*)-dione (11g)**



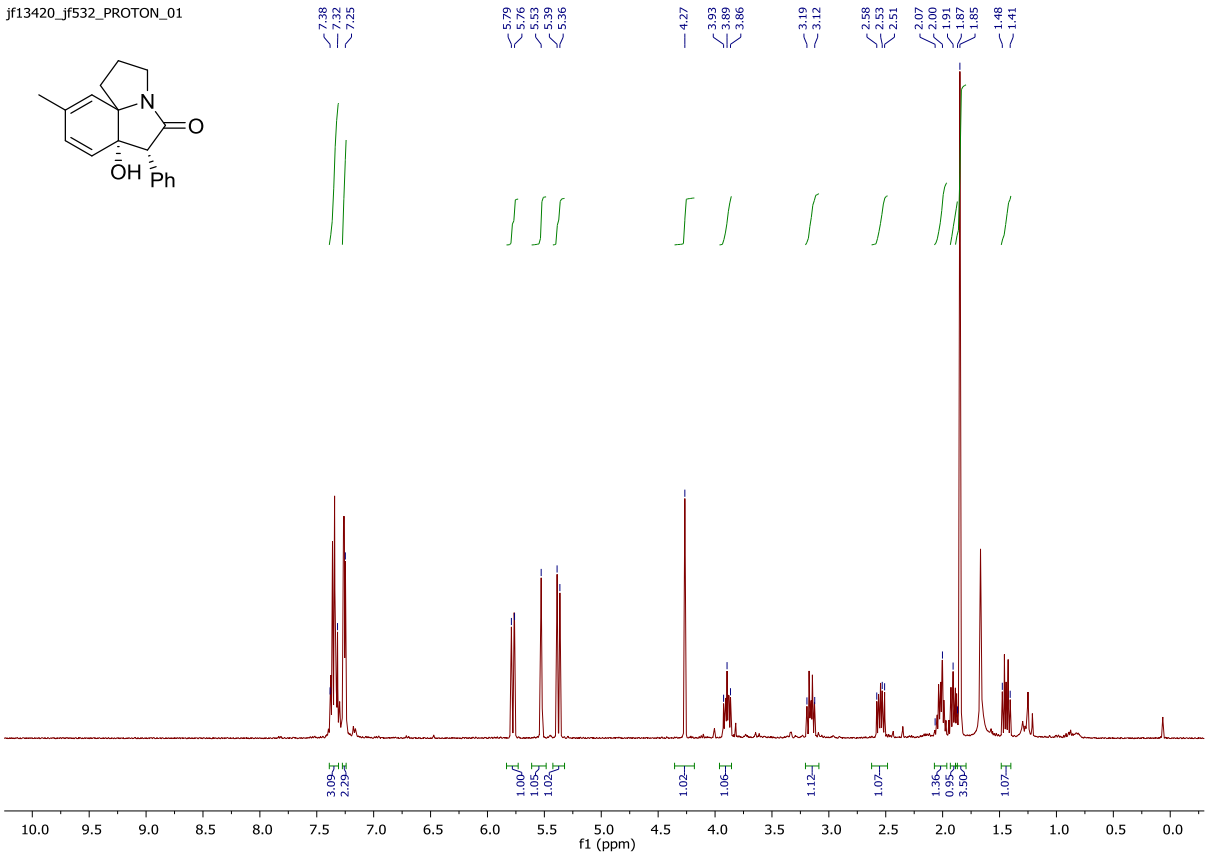


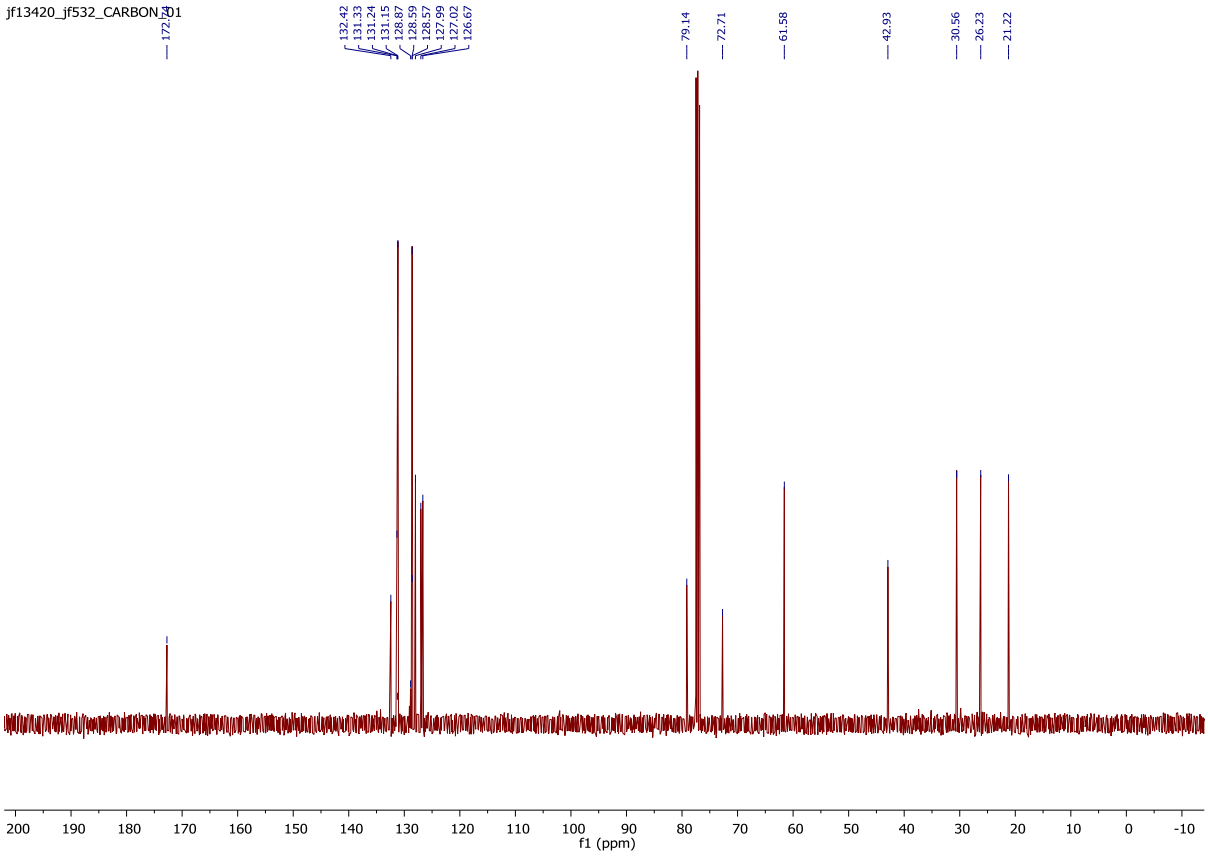
9-methyl-1-(2-phenylacetyl)-1-azaspiro[4.5]deca-7,9-dien-6-one





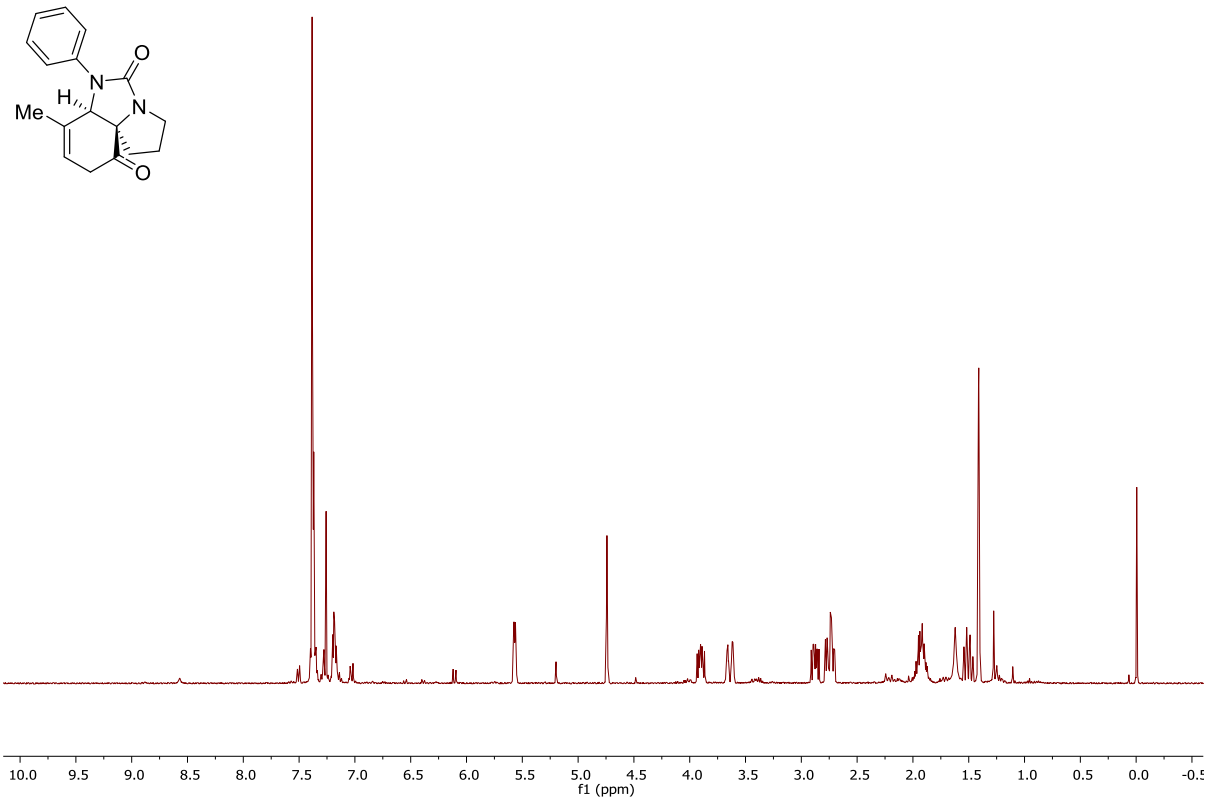
(6R,6aS)-6a-Hydroxy-9-methyl-6-phenyl-2,3,6,6a-tetrahydro-1*H*,5*H*-pyrrolo[2,1-i]indol-5-one (12k)



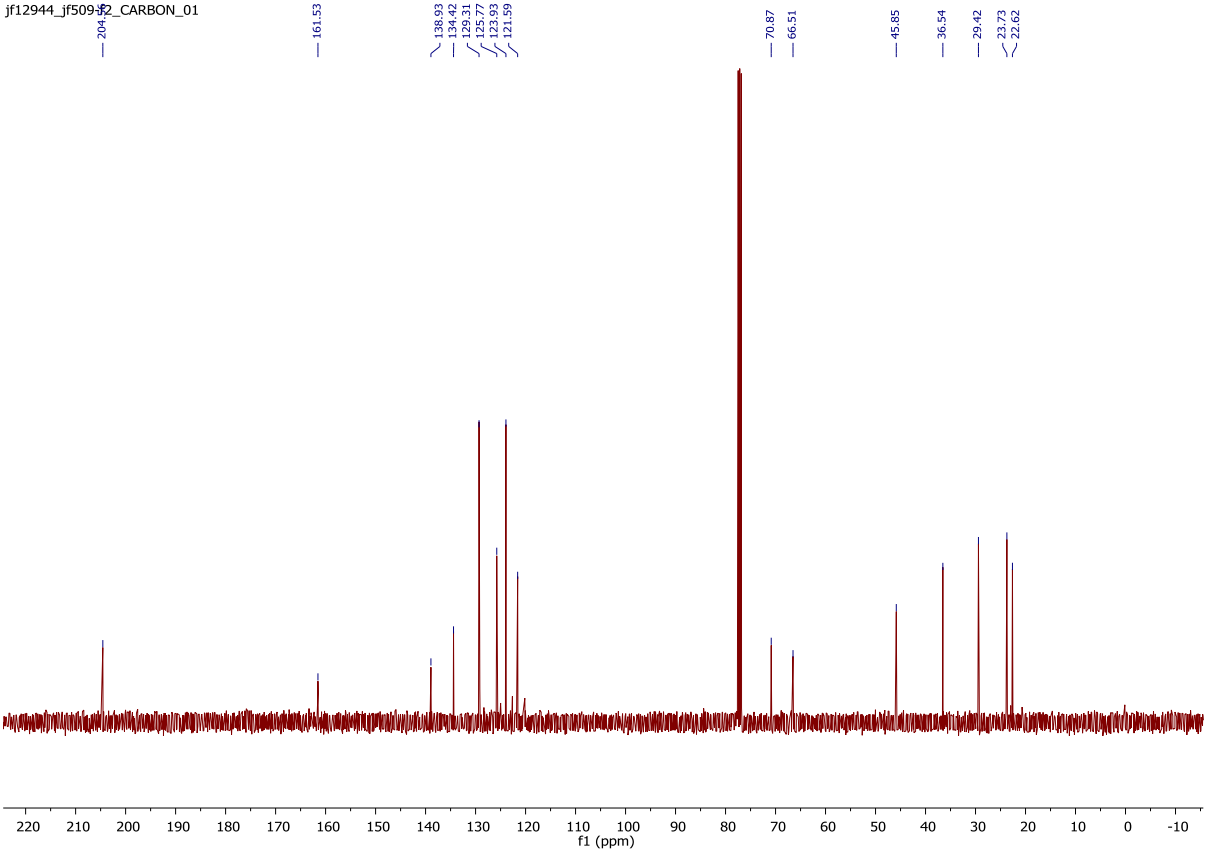


7-methyl-6-phenyl-2,3,6a,9-tetrahydro-1*H*,5*H*-benzo[d]pyrrolo[1,2-c]imidazole-5,10(6*H*)-dione (11k)

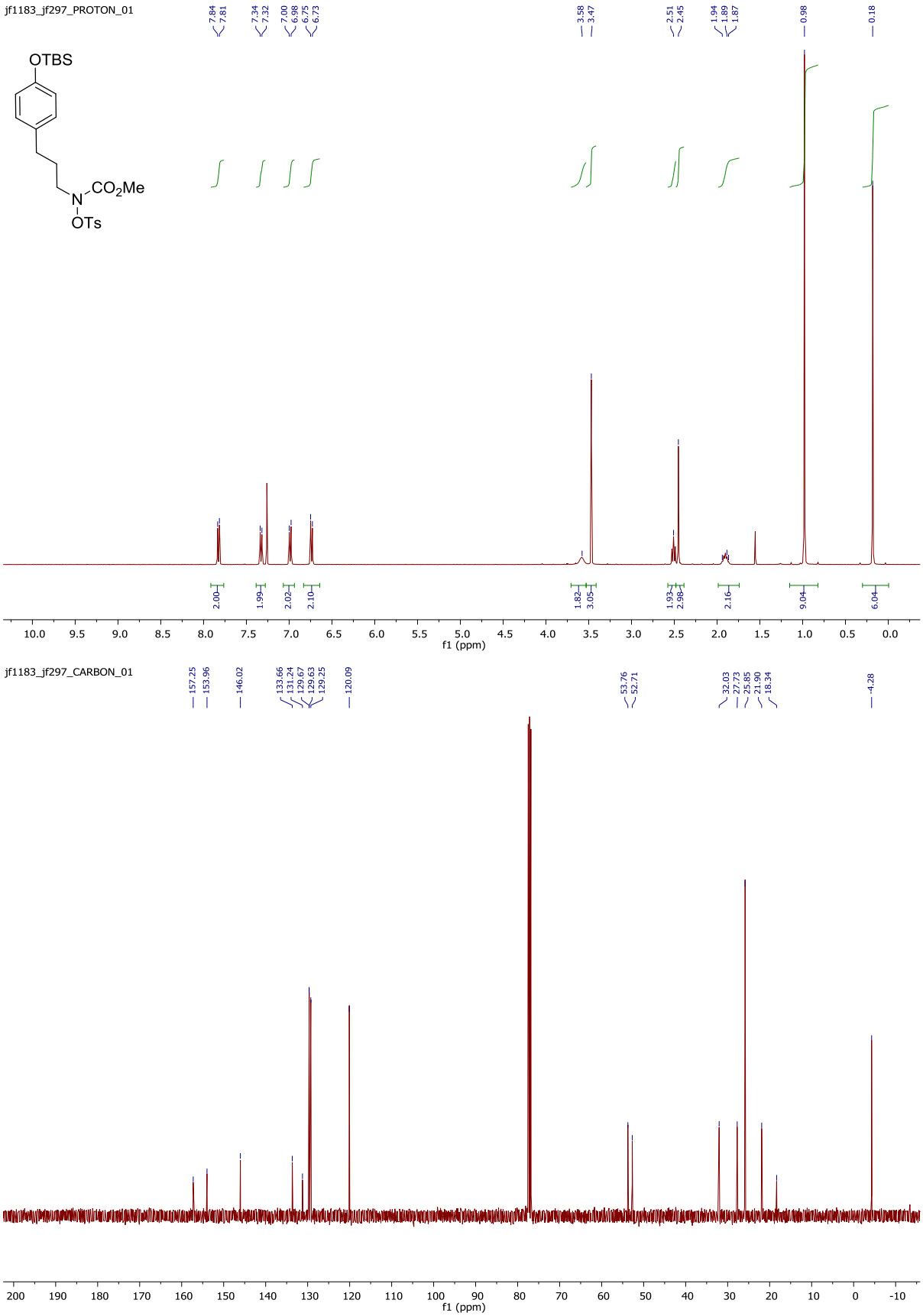
jf12944_jf509-f2_PROTON_01



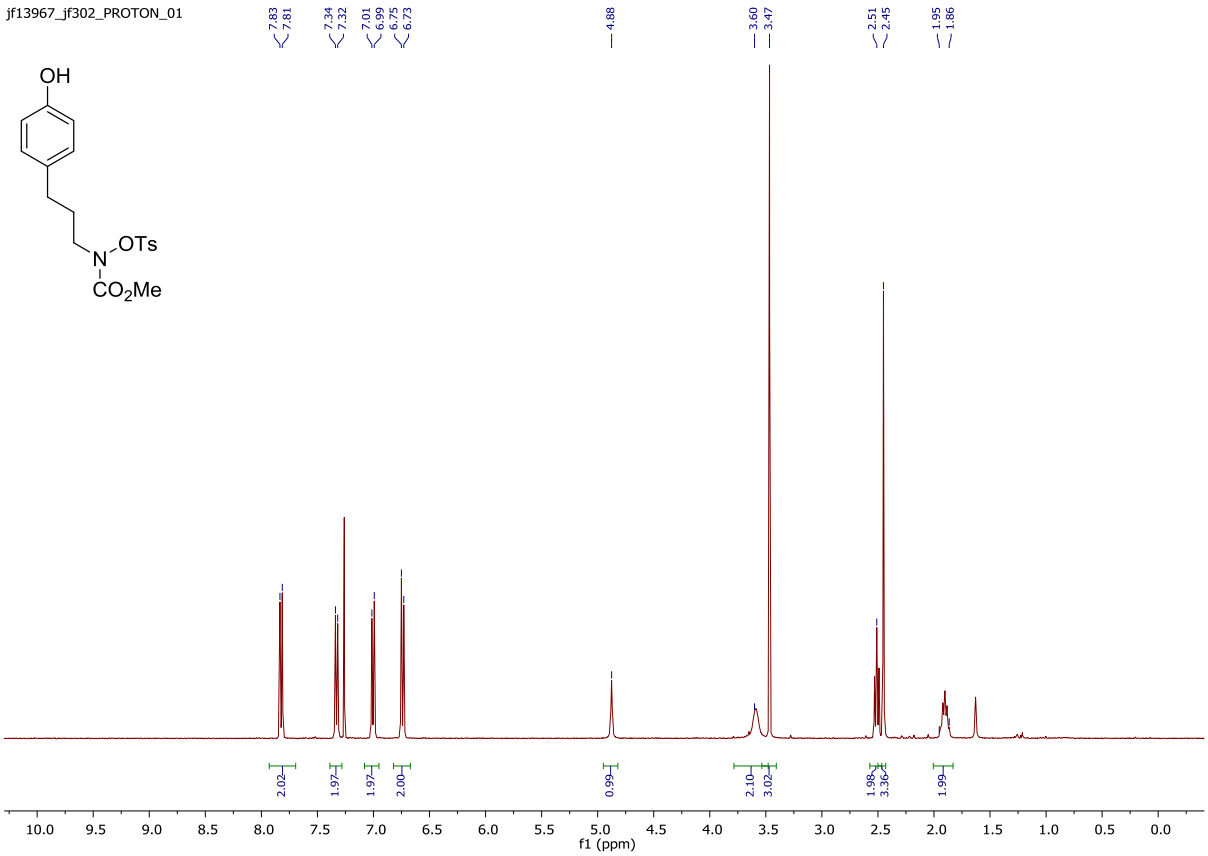
jf12944_jf509-f2_CARBON_01

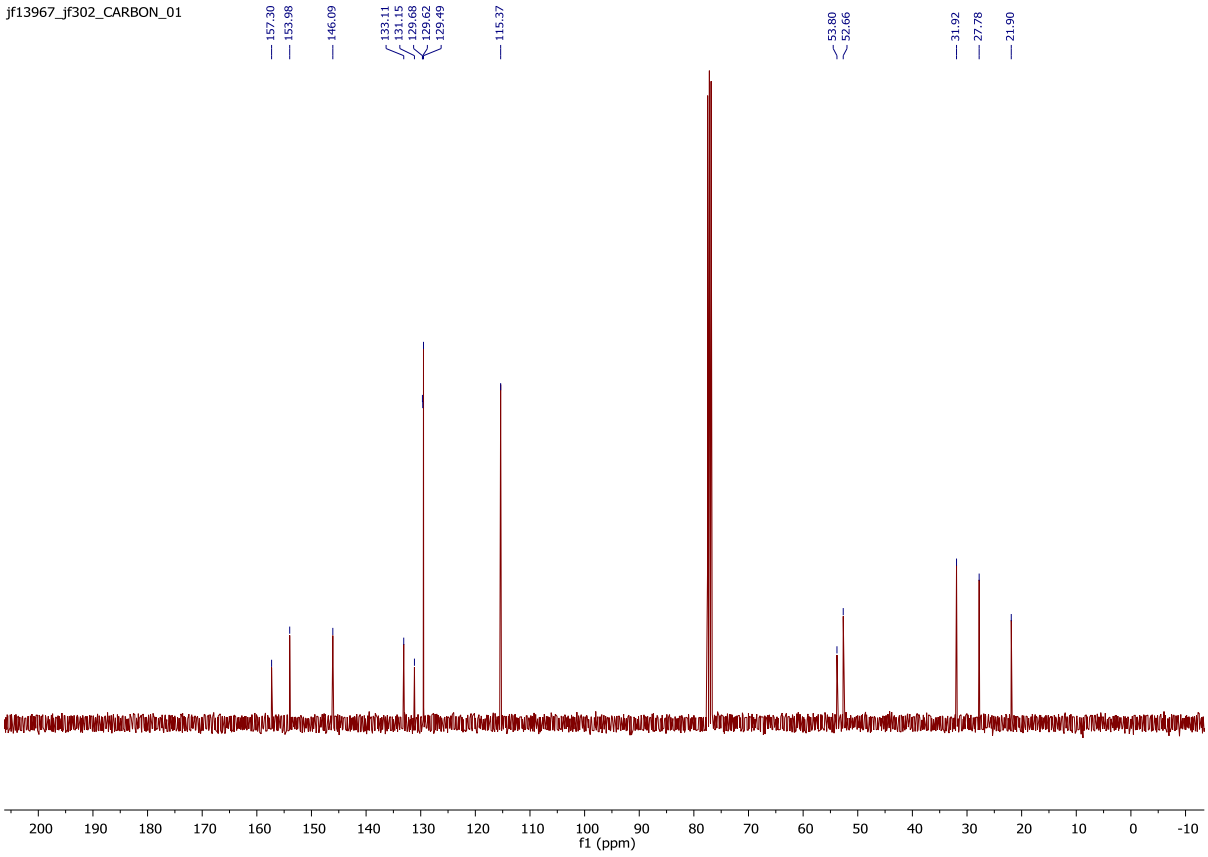


Methyl (3-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)propyl)(tosyloxy)carbamate

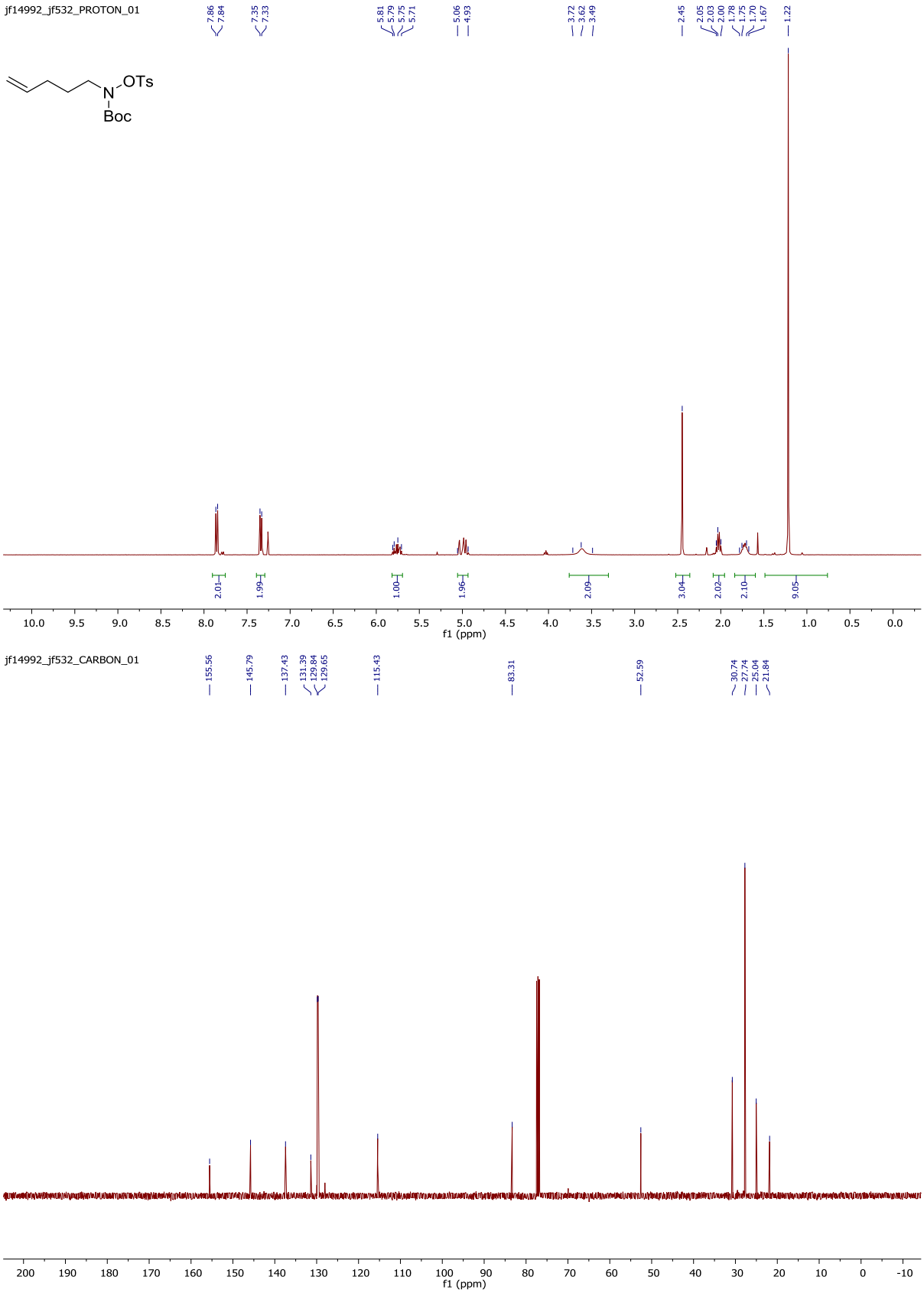


Methyl (3-(4-hydroxyphenyl)propyl)(tosyloxy)carbamate (15)





tert-Butyl pent-4-en-1-yl(tosyloxy)carbamate (17)



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